"A PROSPECTIVE RANDOMISED STUDY ON COMPARISON OF INDUCTION DOSE REQUIREMENTS AND HEMODYNAMIC ALTERATIONS OF MIDAZOLAM-PROPOFOL AND PROPOFOL-PROPOFOL COINDUCTION IN PATIENTS UNDERGOING ELECTIVE GENERAL SURGERY"

Dissertation submitted to

THE TAMILNADU DR. M.G.R.MEDICAL UNIVERSITY

in partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600 003

APRIL 2015

CERTIFICATE

This is to certify that the dissertation entitled, **"A PROSPECTIVE RANDOMISED STUDY ON COMPARISON OF INDUCTION DOSE REQUIREMENTS AND HEMODYNAMIC ALTERATIONS OF MIDAZOLAM-PROPOFOL AND PROPOFOL-PROPOFOL COINDUCTION IN PATIENTS UNDERGOING ELECTIVE GENERAL SURGERY"** submitted by **Dr.S. JAMUNA**, in partial fulfilment for the award of the degree of **Doctor of Medicine** in Anaesthesiology by the **Tamilnadu Dr. M.G.R. Medical University**, Chennai., is a bonafide record of the work done by her in the **INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE**, Madras Medical College and government hospital, during the academic year 2012-2015.

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DECLARATION

I hereby, solemnly declare that this dissertation entitled **"A PROSPECTIVE RANDOMISED STUDY ON COMPARISON OF INDUCTION DOSE REQUIREMENTS AND HEMODYNAMIC ALTERATIONS OF MIDAZOLAM-PROPOFOL AND PROPOFOL-PROPOFOL COINDUCTION IN PATIENTS UNDERGOING ELECTIVE GENERAL SURGERY"** is a bonafide work done by me in the Institute of Anaesthesiology and Critical Care, Madras Medical College and Government General hospital, Chennai, during the Period 2012 to 2015 under the guidance of **Prof.Dr.ESTHER SUDHARSHINI RAJKUMAR, M.D,D.A,** Professor of Anaesthesiology, Institute of Anaesthesiology and Critical Care, Madras Medical College and Government General Hospital, Chennai – 3 and submitted to **The Tamilnadu Dr. MGR Medical University,** Guindy, Chennai – 32, in the partial fulfilment of the requirements for the award of the degree of MD Anaesthesiology (Branch X), examinations to be held on April 2015.

I have not submitted this dissertation previously to any university for the award of degree or diploma.

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Place: Chennai
Date:

ACKNOWLEDGEMENT

I am extremely thankful to **Dr.R.VIMALA,M.D.,** Dean, Madras Medical College & Rajiv Gandhi Govt General Hospital, for her permission to carry out this study.

I am immensely grateful to **Prof. Dr.B.KALA M.D.,D.A.,** Director and Professor, Institute of Anaesthesiology and Critical Care, for her concern and support in conducting this study.

I am extremely grateful and indebted to my guide **Prof.Dr.ESTHER SUDHARSHINI RAJKUMAR, M.D,D.A,** Professor of Anaesthesiology, Institute of Anaesthesiology & Critical Care for her concern, inspiration, meticulous guidance, expert advice and constant encouragement in preparing this dissertation.

I am very grateful to express my sincere gratitude to the Professors, **Prof.Dr.D.GANDHIMATHI MD,DA, Dr.S.ANANTHAPPAN MD, DA, Dr.SAMUEL PRABAKARAN MD.,DA., Dr.R.LAKSHMI M.D., D.A.,** and **Dr.PANKAJAVALLI M.D.,D.A.,** Institute of Anaesthesiology and Critical Care, for their constant motivation and valuable suggestions.

I am extremely thankful to my all Assistant Professors for their guidance and expert advice in carrying out this study.

I am thankful to the Institutional Ethics Committee for their guidance and approval for this study.

My sincere thanks to the statistician, who played an important role during my study

I am thankful to all my colleagues, family and friends for their moral support, help and advice in carrying out this dissertation.

Last but not the least, I thank all the patients for willingly submitting themselves for this study.

Above all I pay my gratitude to the Lord Almighty for blessing me to complete this work.

ABBREVIATIONS

HR	-	Heart Rate
SBP	-	Systolic Blood Pressure
DBP	-	Diastolic Blood Pressure
MAP	-	Mean Arterial Blood Pressure
CMRO2	-	Cerebral Metabolic requirement of Oxygen
LMA	-	Laryngeal Mask Airway
ASA	-	American Society of Anaesthesiologist
SD	-	Standard Deviation
NS	-	Not Significant
S	-	Significant

CONTENTS

A PROSPECTIVE RANDOMISED STUDY ON COMPARISON OF INDUCTION DOSE REQUIREMENTS AND HEMODYNAMIC ALTERATIONS OF MIDAZOLAM-PROPOFOL AND PROPOFOL-PROPOFOL COINDUCTION IN ELECTIVE GENERAL SURGERY

ABSTRACT

BACKGROUND OF STUDY

Co-induction of anesthesia with Midazolam and Propofol with or without opioids can be considered as useful technique of induction of anaesthesia. The aim of the present study was to evaluate the efficacy of priming technique in relation to induction agents. Clinical efficacy in terms of dose reduction and alteration in peri-intubation haemodynamics was compared in Propofol-Propofol and Midazolam -Propofol co-induction groups along with a control group.

METHODS

The study was carried out in 90 patients scheduled for elective general surgery, who were randomly divided into three equal groups. Group I received 2 ml of normal saline(control group), group II received 0.05 mg/kg IV Midazolam and group III received 0.5mg/kg of Propofol. This was followed by IV induction with Propofol 2 minutes later in all the three groups at a predetermined rate till loss of response to verbal commands. Parameters like induction dose requirements and hemodynamic alterations are observed.

RESULTS

Using loss of response to verbal command and tolerance to placement of pace mask as end points, the dose of Propofol required to induce anaesthesia was significantly smaller in group-2 & group-3 (mean Propofol usage was 40.33

and 69.00 respectively) when compared to control group (99.67) the total cost of induction was significantly reduced in the Midazolam co-induction group.

CONCLUSION

We conclude that Midazolam or Propofol predosing were equally effective in reducing the induction dose requirement of Propofol. Midazolam co-induction is more economical than Propofol predosing. Propofol –Propofol coinduction have better hemodynamics than Midazolam-Propofol group.

Key words : Propofol, Midazolam, Auto-co-induction.

INTRODUCTION

For more than 70 years development of intravenous anaesthetics has been an important component of anaesthetic management. Prior to the development of intravenous anaesthesia, inhalation anaesthesia was practised. As Inhalation of gases was unpleasant to some patients, intravenous anaesthesia gained popularity.

Intravenous anaesthesia followed the invention of hypodermic syringe and needle by Alexander wood in 1855.

First successful attempt at intravenous anaesthesia in 1872 by Pierre Cyprien ore by using Chloral hydrate for anaesthetising patients.

Other agents like Chloroform, Chloral hydrate, Ether were also used.

Later the combination of Intravenous Morphine and Scopalamine by Brenfeld in 1916 gained popularity in obstetric anaesthesia. This was known as twilight sleep. But this combination was withdrawn due to side effects.

First Barbiturate named Barbituric acid were discovered in 1864, but it had no sedative action. Then barbiturate which had sedative action was discovered by Fischer von Mering in 1903. Diethyl barbituric acid was the first barbiturate used for induction of anaesthesia. Thiopentone

synthesized in 1932 by Volwiler and Tabern. It was first used clinically by John Lundy and Ralph Waters in 1934, it remains most common induction agent for anaesthesia. Methohexital was used clinically in 1957 by V.K.Stoelting. It was also used for induction of anaesthesia.

According to Lundy General anaesthesia was safer with the use of multiple agents because the dose of particular agent was smaller and fewer side effects were observed.

Then Ketamine was synthesized in 1962 by Stevens. It was used clinically in 1965 by Corssen and Domino and released in 1970.

Ketamine is a unique agent in the armamentarium of anaesthesiologist, as it does not depress the cardiovascular system even in full anaesthetic doses.

Etomidate was introduced in 1973 and it was used for induction of anaesthesia. It produces only minimal hemodynamic depression and it gained popularity in anaesthetising patients with cardiac disease. Adrenal suppression was the major side effect seen with Etomidate.

Then Propofol came into light in 1977. It has achieved widespread use since its introduction. It was a major advance in outpatient anaesthesia because of its short duration of action and rapid recovery profile. Propofol is often administered as anaesthetic agent, with or

without the addition of inhaled anaesthetics. When combined with the analgesic agents such as Opioids, Propofol can provide all components of satisfactory general anaesthesia. Thus Propofol can be used in total intravenous anaesthesia (TIVA).

HISTORY OF PROPOFOL

First developed in 1976 by the Imperial chemical industry .It was originally emulsified into Cremophor and clinical trials were conducted..But it was withdrawn from market due to high number of patients undergoing anaphylactic shock. Then reformulated into an emulsion of Soyabean oil and was released by Astra Zeneca pharmaceuticals in 1986.First clinical trial by Kay and Rolly in 1977, confirmed the potential of Propofol as an anaesthetic induction agent. He used 2%formulations with cremophor and alcohol.

HISTORY OF BENZODIAZEPINES

The Benzodiazepines was extensively used for premedication, induction of anaesthesia and also used for intravenous sedation. Chlordiazepoxide was first Benzodiazepine synthesized in 1957.

Later other Benzodiazepines like Diazepam was synthesized in 1959, Lorazepam was synthesized in 1971 and Midazolam was synthesized in 1976.

METHODS OF GENERAL ANAESTHESIA

General anaesthetics are compounds that induce a reversible loss of consciousness in humans or loss of righting reflex in animals. Clinically it also include the lack of awareness to painful stimuli. General anaesthetics do not act as analgesics and should also not be confused with sedatives.

SITES OF ACTION

General anaesthetics can interrupt central nervous system at different levels like spinal cord, brainstem, cerebral cortex, peripheral sensory neurons. Delineation among action on anatomic sites is difficult, as they act diffusely and inhibit central nervous system. The different components of anaesthesia resulted by the action of anaesthetic agents on different sites.

- Immobilisation in response to surgical incision is due to action on spinalcord.
- Sedative action is due to involvement of the neuronal pathway in endogenous sleep. Propofol acts on GABA A in tuberomamillary neurons results in its sedative effect. Dexmedetomidine, an alpha agonist acts on locus ceruleus resulting in its sedative effect. Inhalation anaesthetics depresses the excitability of thalamic neurons which acts as a locus for its sedative action.

- Amnesia results from depression of hippocampal neurotransmitter which acts as a locus for its amnesic effects.

MECHANISM OF ACTION OF DRUGS

LIPID THEORY

At 20^{th} century, Overton and Meyer described, General anaesthetics exert their action by acting on the plasma membrane.

This was supported by evidence that the potency of the drug has a direct, positive correlation with the lipid solubility of the blood. The mechanism of action was proposed to be increased fluidity of the membrane. The interpretation of the Overton and Meyer finding has been challenged and discredited.

CELLULAR MECHANISM

General anaesthetics have two physiological effects at cellular level. First, inhalation anaesthetics hyperpolarize neurons. Thereby reduced excitability in a postsynaptic neuron diminishes the likelihood of action potential initiated in response to neurotransmitter release.

Second, at anaesthetic concentration, both intravenous and inhalation anaesthetic agents have effects on synaptic transmission and least action on action potential generation and propagation.

Inhalation anaesthetic agents inhibits excitatory synapses and enhances inhibitory synapses by their action on presynaptic and postsynaptic sites.

- In postsynaptic site – it alters the response to released neurotransmitters via its action on receptors.
- In presynaptic site – it decreases the neurotransmitter release by producing a small decrease in presynaptic action potential amplitude. This results in greater reduction in calcium influx in presynaptic site which is responsible for neurotransmitter release.

Intravenous anaesthetics acts predominantly at synapses. It has its action profoundly on postsynaptic site. It acts predominantly by enhancing the release of inhibitory neurotransmitter. Ketamine is the only intravenous drug which inhibits excitatory neurotransmitter.

MOLECULAR MECHANISM

It is postulated that general anaesthetics exert their action through ion channels.

The relative roles of different receptors is still under much debate, but evidence has emerged for some targets being involved with particular anaesthetics.

Multiple anaesthetics have been found to affect the inhibitory $GABA_A$ receptor, including Propofol, Thiopental and Isoflurane

In clinical concentrations, inhalation anaesthetic agents enhance the capacity of Glycine to activate Glycine gated chloride channels. It inhibits neurotransmitter release at brain and spinalcord.

In subanaesthetic concentration inhalation anaesthetics inhibits neuronal nicotinic acetylcholine receptors. This mediates analgesia, amnesia but not able to mediate immobilization for noxious stimuli.

Only anaesthetic agents that donot have effect on GABA, Glycine receptors are Ketamine, Nitrous oxide, Cyclopropoane and Xenon. They act through NMDA receptors.

Other channels are

- Halogenated inhalation anaesthetic agents acts on a class of potassium channel. These are two pore domain channels. These channels are responsible for setting the resting membrane potential and may act as locus through which hyperpolarization of neurons occurs.
- Inhalation anaesthetics may requires a protein complex. These protein complexes (synaptin, synaptobrevin, syntaxin) are involved in synaptic neurotransmitter release. This may be the cause for

presynaptic inhibition of neurotransmitter release in hippocampus, which is the site of action for amnesia.

TWO MODES OF ADMINISTRATION (Induction)

1. Inhalation technique
2. Intravenous technique

GUEDEL'S STAGES OF ANAESTHESIA:

There are four stages in general anaesthesia

Stage I (Stage of analgesia or disorientation):

From beginning of induction of general anesthesia to loss of consciousness.

Stage II (Stage of excitement or delirium):

From loss of consciousness to onset of automatic breathing. During this stage eyelash reflex disappear but other reflexes remain intact and coughing, vomiting and struggling may occur.

Respiration can be irregular with breath-holding.

Stage III (stage of surgical anesthesia):

From onset of automatic respiration to respiratory paralysis. It is divided into four planes:

Plane I - From onset of automatic respiration to cessation of eyeball movements.

During this period Eyelid reflex and swallowing reflex disappears, marked eyeball movement may occur but conjunctival reflex is lost at the bottom of the plane

Plane II - From cessation of eyeball movements to beginning of paralysis of 10ntercostals muscles.

- Laryngeal reflex is lost although inflammation of the upper respiratory tract increases reflex irritability
- Corneal reflex disappears
- Secretion of tears increases (a useful sign of light anesthesia)
- Respiration is automatic and regular
- Deep breathing as a response to skin stimulation disappears.

Plane III - From beginning to completion of 10ntercostals muscle paralysis. Diaphragmatic respiration persists but there is progressive 10ntercostals paralysis

- Pupils dilated and light reflex is abolished.
- The laryngeal reflex lost in plane II can still be initiated by painful stimuli arising from the dilatation

of anus or cervix. This was the desired plane for surgery when muscle relaxants were not used.

Plane IV - From complete intercostal paralysis to diaphragmatic Paralysis. However, xenon and nitrous oxide are thought to have no effect here.

Stage IV:

From stoppage of respiration till death.

Anaesthetic overdose can cause medullary paralysis with respiratory arrest and vasomotor collapse. Pupils are widely dilated and muscles are relaxed.

In 1954 Joseph F. Artusio further divided the first stage in Guedel's classification into three planes

- 1st plane –The patient does not experience amnesia or analgesia
- 2nd plane- The patient is completely amnesic but experiences only partial analgesia
- 3rd plane- The patient has complete analgesia and amnesia

INDUCTION

Induction is a term that refers to the first stage of anaesthesia, Stage 1, prior to reaching a depth suitable for surgery i.e. Stage 3.

The speed of induction depends on the time taken for the drug to reach an effective concentration in the brain. Different anaesthetic compounds reach different compartments of the body, such as fatty tissue, muscle etc., at different rates. Hence, different compounds have different rates of induction.

Intravenous anesthetics like Thiopental have been used for induction. Propofol is now the most widely used intravenous induction agent.

PRINCIPLES OF SURGICAL ANAESTHESIA

1. Minimizing the potentially deleterious effects of anesthetic agents and techniques.
2. Sustaining physiologic homeostasis during surgical procedures that may involve major bloodloss, tissue ischemia, reperfusion of ischemic tissue, fluid shifts, exposure to a cold environment, and impaired coagulation.
3. Improving postoperative outcomes by choosing techniques that block or treat components of the surgical stress response, which may lead to short- or long-term sequelae.

ELIMINATION OF ANAESTHETIC AGENTS

Volatile anaesthetics are eliminated in the terminal phase via the lungs. A low blood:gas partition coefficient is therefore necessary for quick removal of the anaesthetic. When the oil:water coefficient is high, there will be little anaesthetic in the blood, so elimination will be slow, giving a prolonged hangover effect.

Intravenous and intramuscular drugs are eliminated by metabolic pathways in the liver. It is not uncommon to produce toxic metabolites (e.g. chloroform).

SYNERGISM

In **Greek synergos- means working together**

Working together of two or more drugs to produce an effect greater than sum of their individual effect is known as synergism.

In our study we took the synergistic action of Propofol and Midazolam. Both drugs act on GABA A receptor. But they act at different sites. GABA is major central nervous system inhibitory neurotransmitter. It produces fast inhibitory synaptic transmission.

Primary target of general anaesthesia is GABA receptor, whose inhibitory action is responsible for hypnosis, amnesia, anxiolysis.

Histaminergic neurons in posterior hypothalamus (tuberomamillary neurons) control wakefulness. Their silencing through GABA induces sleep.

Propofol and Midazolam have synergistic action in producing hypnosis.

GABA RECEPTOR

This receptor is a pentameric structure. These are the class of receptors that respond to neurotransmitter GABA.

Types of receptor

GABA A , GABA B,GABA C

GABA A

- Its a ligand gated ion channel.
- Also known as ionotropic receptors.
- Fast responding GABA receptors
- Belongs to members of family of cys loop ligand ion channel. Members include nicotinic receptors, glycine, 5HT3 receptors. These form characteristic loop formed by disulphide bond between 2 cystine residues
- These are blocked by Biculline

GABA B

- Its a G protein coupled receptor.
- Also called metabotropic receptors
- Slow responding GABA receptors
- These are not blocked by Biculline

GABA C

- Its a allosteric modulator of GABA A

STRUCTURE

Contains 5 subunits around a central core. Each subunit comprises four transmembrane domain with both N & C terminus located extracellularly. There are 6 types of subunits

- Alpha 1,2,3,4,5,6
- Beta 1,2,3
- Gamma 1,2,3
- Others are delta, rho, theta

These five subunits can bind in different ways. Most common type of receptor contains 2 alpha, 2 beta subunits.

Ligand GABA is endogenous compound that causes receptor to open resulting in flow of Chloride ions. Endogenous ligand that binds to Benzodiazepine site is Inosine.

While majority of GABA receptors (alpha 1,2,3,5) are Benzodiazepine sensitive there are subunits (alpha4,6)that are not Benzodiazepine sensitive but sensitive to neurosteroid and ethanol.

Different Benzodizepines have different affinity for GABA

- Those binds to Alpha 1 & 5 results in sedation, amnesia
- Those binds to Alpha 2 & 3 results in anxiolysis
- Anticonvulsant activity occurs by binding to any receptors. Most commonly anticonvulsant binds to alpha 2 thereby reducing the side effects like amnesia.
- Those binds to Beta 3 results in respiratory depression
- Those binds to Beta 3 and 2 results in hypnosis

Binding sites:

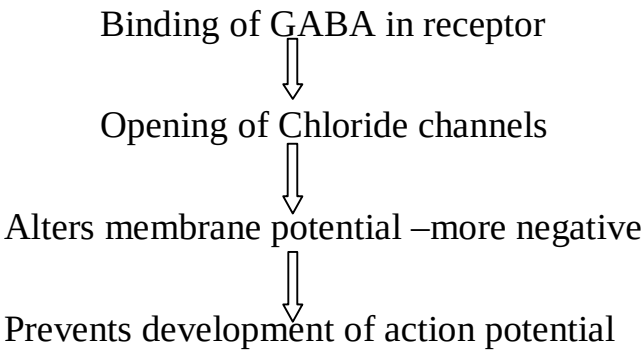
- GABA binds between alpha and beta subunit
- Benzodiazepines binds between alpha and gamma subunit
- Propofol binds in beta subunit
- Barbiturates binds at different site to GABA

Both Propofol and Midazolam are GABA facilitatory Midazolam causes higher affinity to GABA, which results in potentiation of inhibitory effect of available GABA Propofol decreases the rate of dissociation of inhibitory neuron GABA thereby increases the duration of opening of chloride channel.

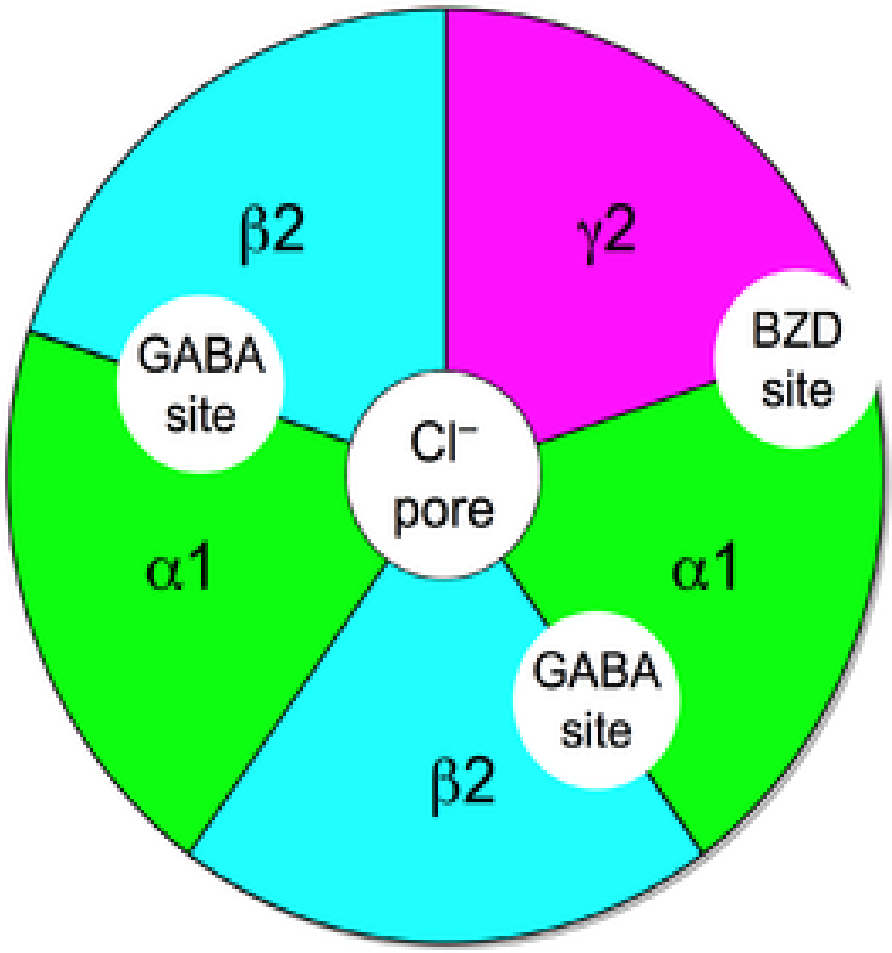
Benzodiazepines results in burst of Chloride channel to open. Barbiturates increases the duration of opening of channels. So Benzodiazepines and Barbiturates act synergistically.

Mechanism of action

GABA binds to GABA receptor extracellularly resulting in opening of Chloride channel. Entry of Chloride ions into cell results in more negativity of membrane potential. When membrane potential reaches around -65mv it results in hyperpolarisation thereby action potential does not develops.

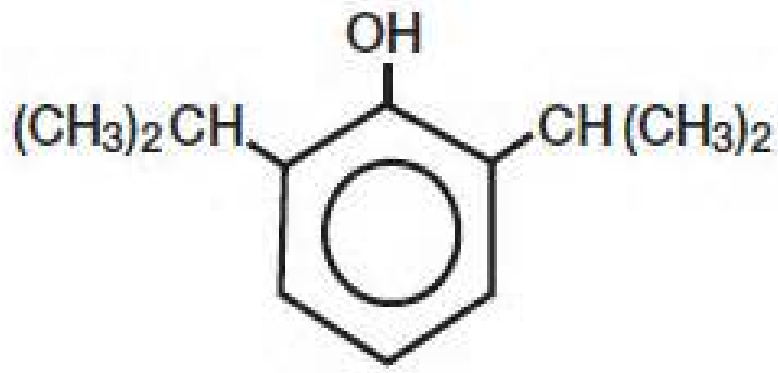


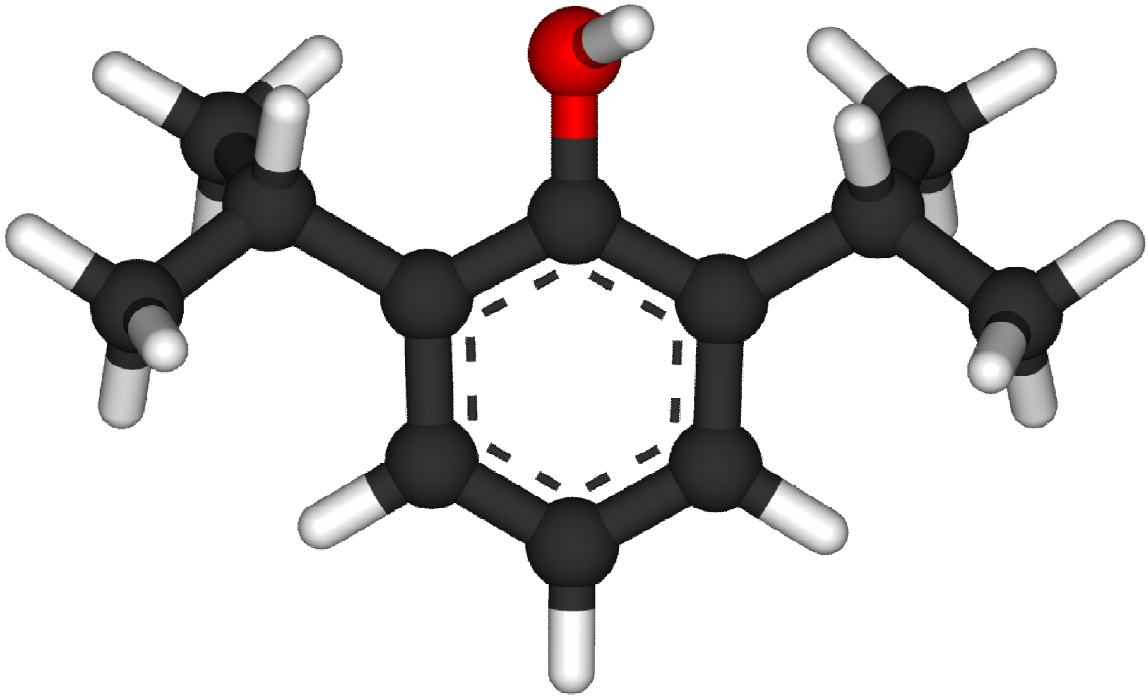
STRUCTURE OF GABA RECEPTOR



PROPOFOL

MOLECULAR STRUCTURE OF PROPOFOL





Is a substituted isopropylphenol(2,6 DIISOPROPYLPHENOL)

Altering its side chain length influences its potency, induction, recovery.

Not a chiral compound.

PREPARATION

Its a insoluble drug requires a lipid vehicle for emulsification

CURRENT FORMULATIONS - Contains 10% soyabean oil (as oil phase) &1.2%egg lecithin (for emulsification). It is made of long chain triglycerides and 2.25%glycerol

This combination promotes bacterial growth and increase in triglycerides. Mixing with other drugs can result in coalescence of oil droplets with risk of pulmonary embolism. These demerits resulted in the introduction of different formulations.

With respect to modification in preservatives Diprivan and Generic Propofol came to market.

DIPRIVAN - Contains 0.005% disodium edenate with NaOH as preservative (pH 7 – 8.5)

GENERIC - Contains sodium metabisulphite 0.25mg/ml as Preservative (pH 4.5-6.5)

AMPOFOL - **C**ontains 5% soyabean oil & 0.6% egg lecithin

Low lipid emulsion formulations

Not requires preservative

Produces pain on injection

Then as an alternative to emulsion formulations and to avoid side effects of previous formulations Aquavan was introduced.

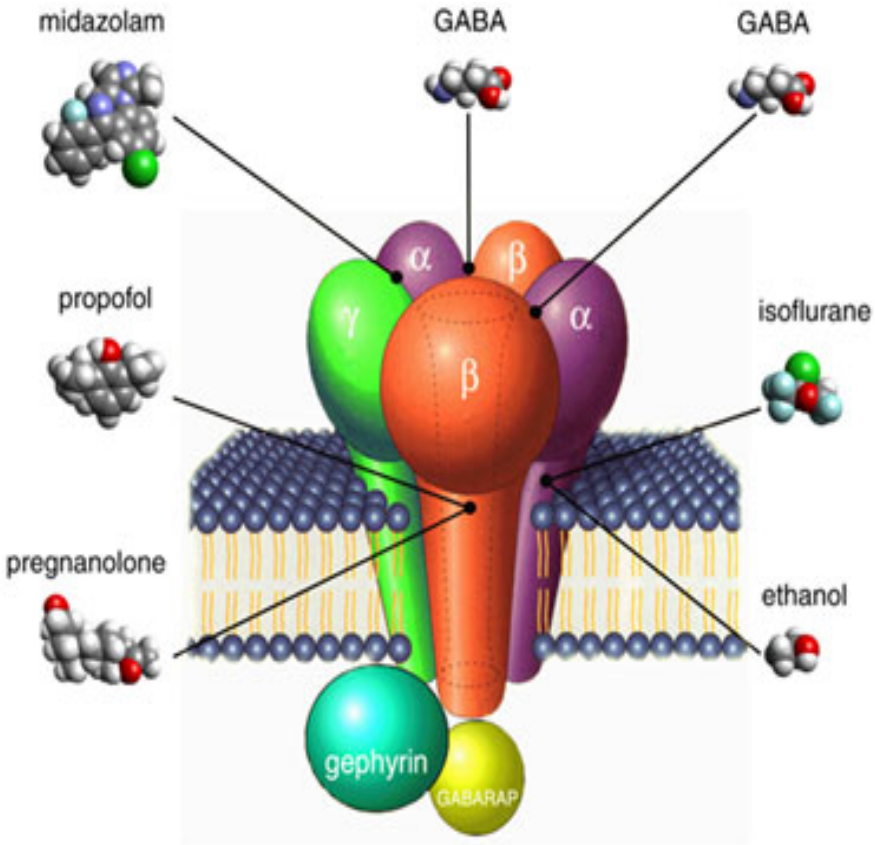
AQUAVAN - Is a prodrug which acts by cleaving groups to parent compounds(phosphate monoesters, hemisucccinates) Propofol is liberated after hydrolysis by endothelial surface alkaline Phosphatases. Thereby it increases water solubility (alternative to emulsion formulation).This drug has larger volume of distribution and higher potency.

ALONG WITH CYCLODEXTRINS - Is an injectable form of Propofol. It is a nonlipid formulations. It is a ring sugar molecule. After injection propofol migrates out of it into the blood.

MECHANISM OF ACTION

GABA A FACILITATORY

GABA receptor on activation increases transmembrane conductance resulting in hyperpolarisation of postsynaptic cell membrane and functional inhibition of post synaptic neuron.



PHARMACOKINETICS

ABSORPTION - Only intravenous

DISTRIBUTION - Rapid onset due to high lipid solubility

Rapid recovery with minimal residual

Effects Less hang over so used in day Care

BIOTRANSFORMATION- Both hepatic & extrahepatic

IN LIVER : PROPOFOL undergoes ring hydroxylation by

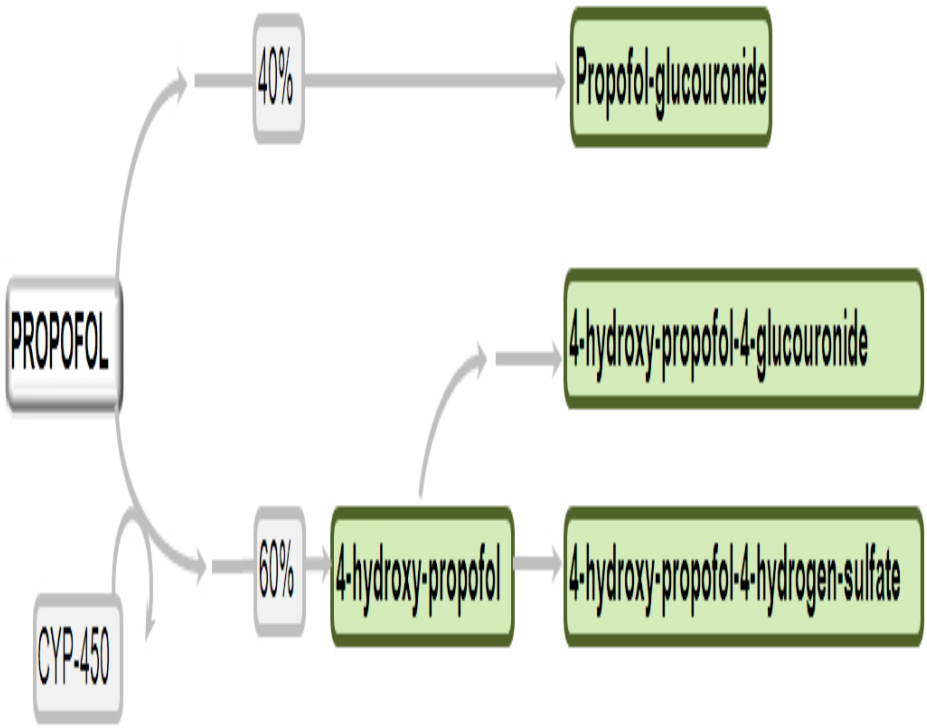
cytochrome p450 and get converted to 4 hydroxypropofol (it has 1/3 hypnotic effect of propofol).

4 hydroxypropofol then undergoes glucuronidation or sulfation into inactive metabolites and excreted through urine.

IN LUNGS : Uptake of Propofol occurs and get transformed to

2,6 di isopropylphenol 1,4 quiniol and released back to circulation.

MAJOR METABOLIC PATHWAY OF PROPOFOL



PLACENTAL CIRCULATION : Crosses placenta but rapidly cleared from neonatal circulation.

DOSAGE :

INDUCTION OF ANAESTHESIA – 1.5 -2.5mg/kg iv

IV INFUSION RATES : For sedation 25-75mic/kg/min

For hypnosis 100-200 mic/kg/min

ELIMINATION HALFLIFE : 0.5 – 1.5hours

CONTEXT SENSITIVE HALF TIME

Less than 40 mins for infusion of 8 hours

VOLUME OF DISTRIBUTION : 3.5 – 4.5 l/kg

CLEARANCE : 30 – 60 ml/kg/min

EFFECTS OF ORGAN SYSTEMS

CENTRAL NERVOUS SYSTEM

- Propofol decreases CMRO2, cerebral blood flow, intracranial pressure.
- Its antioxidant property may be the reason for its neuroprotective behaviour.
- Cerebral autoregulation is not affected by Propofol.
- At equidoses it produces same degree of memory impairment as Midazolam, whereas Thiopentone has milder effect.
- EEG changes shows similar to Thiopentone, causing burst suppression in high doses.
- Induction of Propofol is occasionally accompained by excitatory motor activity due to its subcortical glycine antagonism
- Development of tolerance to Propofol usage is not seen.

CARDIOVASCULAR SYSTEM

- Fall in blood pressure is greater compared to thiopentone. This is due to inhibition of sympathetic activity that results in loss of vasomotor tone leading to vasodilatation and due to its negative

ionotropic effect which is seen due to inhibition of transsarcolemmal calcium influx.

- However Sympathetic response to intubation reverses the blood pressure effects of Propofol.
- Compared to Thiopentone, Propofol blunts the pressor response to laryngoscopy.
- It blunts baroreceptor reflexes so compensatory increase in heart rate does not occurs
- Bradycardia and asystole can occasionally occur. This is due to greater predominance of Propofol on inhibition of sympathetic system.
- Propofol induced bradycardia is treated with beta agonist
- Hypotensive effects are exaggerated in hypovolemic patients, elderly,compromised left ventricular function.
- Also exaggerated when given in large doses and rapid injections.

RESPIRATORY SYSTEM

- Dose dependent depression of ventilation is seen, as it inhibits hypoxic ventilatory drive and also depresses normal response to hypercarbia.
- Apnea occurs in 25-35%

- Hypoxic pulmonary vasoconstriction is not inhibited by Propofol.
- It attenuates vagal induced bronchoconstriction.
- Propofol induced depression of airway reflexes is greater than Thiopentone proves useful in intubation/LMA insertion in absence of paralysis.

HEPATIC AND RENAL SYSTEM

- Can be used in cirrhotic, renal failure patients
- Prolonged infusion can produce hepatocellular injury, rhabdomyolysis
- Urine may appear Green reflecting the presence of phenol or may appear cloudy due to crystallization of uric acid. This appearance in urine is not detrimental.

INTRAOCULAR PRESSURE

- It decreases intraocular pressure

USES

- **Induction of anaesthesia**

Dose of Propofol for induction in healthy adults is 1.5 – 2.5 mg/kg iv. Unconsiousness is produced when the Propofol blood level reaches 2 to 6mic/kg. Children requires higher induction dose of Propofol reflecting a larger central distribution and higher clearance rate whereas elderly people requires lower induction dose reflecting smaller central distribution and decreased clearance rate.

- **Intravenous sedation**

The short effect site equilibration time and short context sensitive half time of Propofol makes it a titratable drug for intravenous sedation. The rapid recovery without residual sedation makes it suitable for day care surgery. For conscious sedation 25-100 mic/kg/min iv dose of Propofol is needed.

- **Maintainance of anaesthesia**

Though Propofol is useful for ambulatory anaesthesia, its usage in long term surgery greater than two hours for maintenance of anaesthesia is questionable due to its high cost. Some found no difference in using Propofol as maintenance drug compared with inhalation agents.

- **Antiemetic**

Propofol reduces the incidence of post operative nausea and vomiting and also chemotherapy induced vomiting. Propofol in subhypnotic dosage of around 10-15 mg iv acts as an antiemetic. The mechanism of its antiemetic action is unclear. The antiemetic efficacy may be due to depression of subcortical areas or direct depression of vomiting centre.

- **Antipruritic**

Pruritis associated with intrathecal Opioids can be attenuated by Propofol. Dosage of 10mg iv is used as antipruritic. Propofol ability to depress the spinal cord activity is responsible for its antipruritic activity, as intrathecal Opioids produce pruritis by segmental activation within spinal cord.

- **Attenuation of bronchoconstriction**

Propofol attenuates vagal induced bronchoconstriction. Thereby comparing to Thiopentone it decreases the prevalence of wheezing in asthmatic and healthy patients after induction and intubation. Preservative like metabisulphite can induce bronchoconstriction and such preparations must be avoided.

SIDE EFFECTS

- Allergic reaction

  Phenyl nucleus and diisopropoyl sidechain are the allergic components in Propofol.

- Substance abuse
- Bacterial contamination

  Propofol supports the growth of e.coli, pseudomonas. Therefore to prevent contamination aseptic precaution to be taken while handling. Immediately after opening the vial the contents should be drawn to a sterile syringe and it should be discarded if not used within 6 hours.

- Pain on injection

  Pain on injecting Propofol is reduced by selecting a larger vein or adding 1 ml of 2%lignocaine to 18 ml of Propofol or addition of Opioids or changing the carrier fat emulsion composition.

- Hypertriglyceridemia, pulmonary embolism
- Lactic acidosis due to PROPOFOL INFUSION SYNDROME

It occurs due to cytopathic hypoxia in those receiving more than 75 mic/kg/min more than 24 hours. When there is unexplained tachycardia or increased anion gap in patients with Propofol infusion suspect lactic acidosis. The metabolic acidosis is reversible on discontinuation of infusion when diagnosed in early stages.

BENZODIAZEPINES

The term Benzodiazepines refers the portion of benzene ring fused to a seven membered diazepine ring.It is a 5 aryl 1,4 benzodiazepine structure.

It has 5 pharmacological effects. Anxiolysis, Anticonvulsant actions, Anterograde amnesia, sedation, spinal cord mediated skeletal muscle relaxation.

Compared to Barbiturates, they have less tendency to produce tolerance, abuse and greater margin of safety after overdose. Benzodiazepines not induce hepatic microsomal enzymes. Thus it replaces Barbiturates for preoperative medication and sedation during monitored anaesthesia care. First Benzodiazepine was used in 1960. It was Chlorodiazepoxide.

CLASSIFICATION OF BENZODIAZEPINES

ANXIOLYTICS

- Diazepam
- Clobazepam
- Oxazepam
- Alprazolam
- Lorazepam

HYPNOTIC

- Nitrazepam
- Flunitrazepam
- Estazolam
- Triazolam

ANTIEPILEPTIC

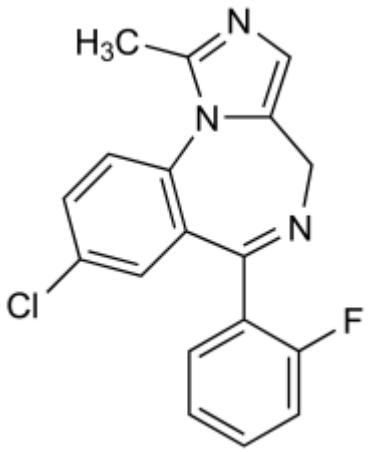
- Clonazepam

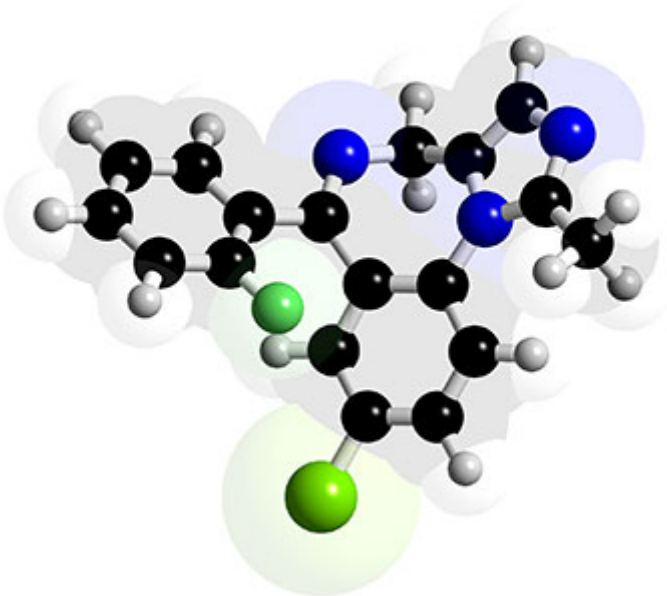
ANAESTHETIC USAGE

- Midazolam

MIDAZOLAM

MOLECULAR STRUCTURE OF MIDAZOLAM

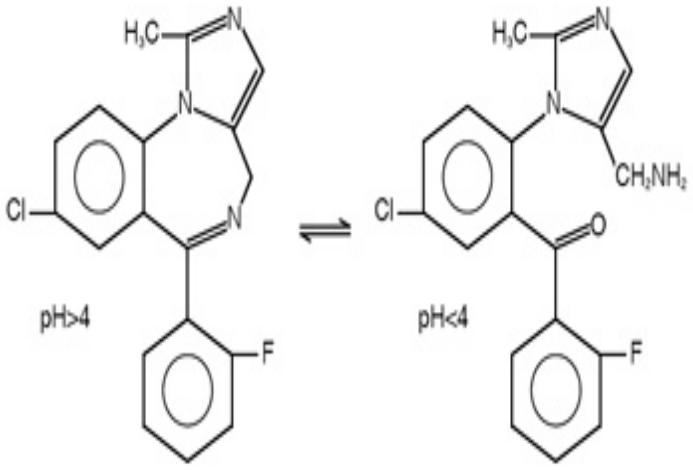




- Developed by HOFFMANN-LA-ROCHE IN 1970s.
- It is a water soluble benzodiazepine.
- It has imidazole ring in its structure which gives stability in aqueous solution and for rapid metabolism.
- It is the most commonly used benzodiazepine.

COMMERCIAL PREPARATION

- Pk 6.15
- Acidic pH 3.5
- Midazolam characterised by pH DEPENDENT RING OPENING phenomenon
- pH < 4 results in opening of ring which makes it water soluble
- pH > 4 results in closure of ring which makes it lipid soluble



Its water soluble property obviates the need of solubilising preparation which is produces veno irritation. So Midazolam injection produces no discomfort.

It can be mixed with acidic salts.

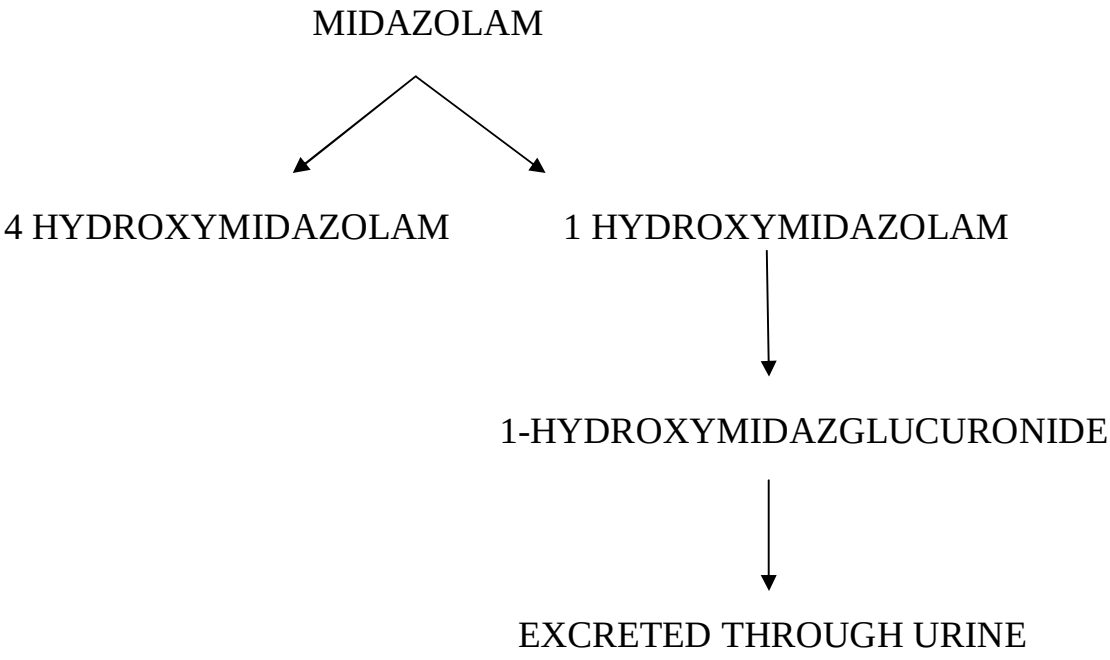
PHARMACOKINETICS

ABSORPTION	–	Oral, im, iv. It undergoes first pass metabolism.
DISTRIBUTION	–	Lipid soluble thereby crosses blood brain barrier. But its slow effect site equilibration time (0.9-5.6 min) needs sufficient spacing between doses for its peak action to take place.
VOLUME OF DISTRIBUTION	–	1-1.5 l/kg
ELIMINATION HALF TIME	–	1-4 hours
CLEARANCE	–	6-8 ml/kg
PROTEIN BINDING	–	96-98%

Short duration of action of Midazolam is due to its lipid solubility, redistribution and rapid hepatic clearance.

BIOTRANSFORMATION

Midazolam is metabolised in liver and small intestine by cytochrome P450 into 4 hydroxymidazolam which is an inactive metabolite and 1hydroxymidazolam which is one half (1/2) potent as parent drug. This undergoes conjugation to form 1-hydroxymidazglucuronide then excreted in urine.

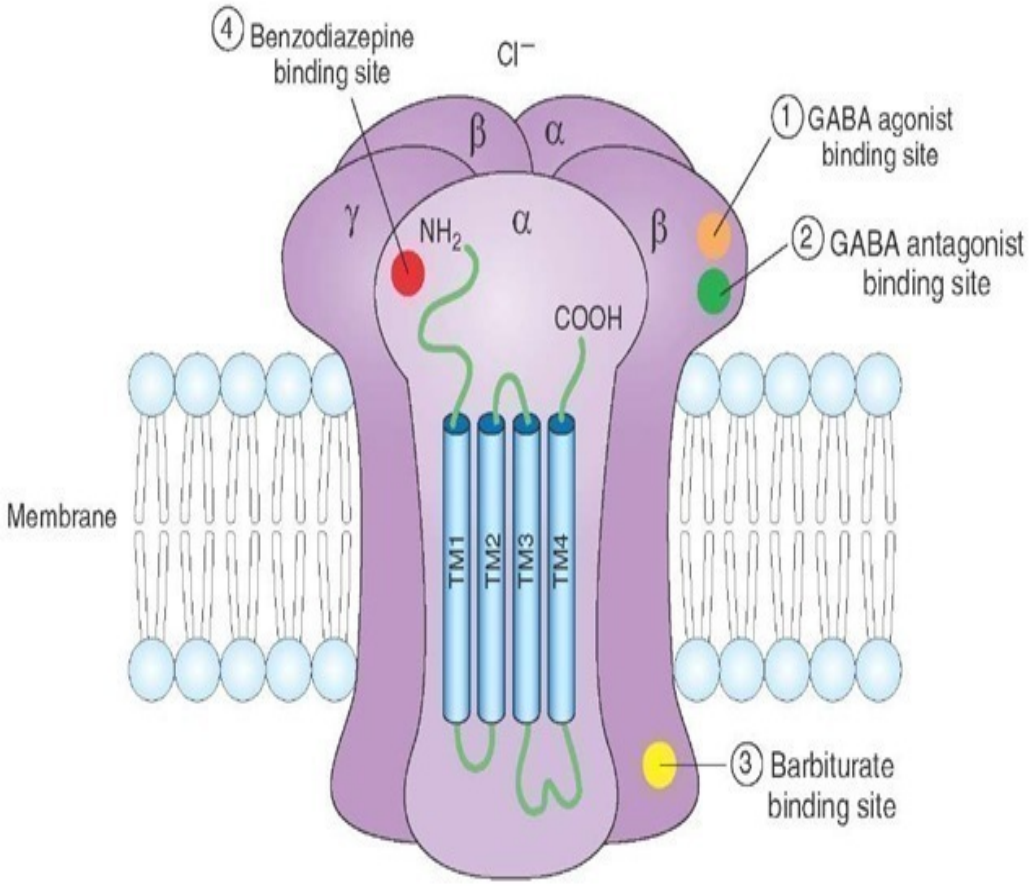


MECHANISM OF ACTION

GABA A FACILITATORY

Action on alpha subunit 1 is responsible for its sedative effect

Action on alpha subunit 2 is responsible for its anxiolysis



EFFECTS ON ORGAN SYSTEM

CARDIOVASCULAR SYSTEM

- It decreases systemic vascular resistance thereby decreases blood pressure.
- The effects on blood pressure is related to its plasma concentration. There is a ceiling effect above which little change in blood pressure occurs.
- Cardiac output is not altered. So Midazolam can be used in congestive cardiac failure patients.
- It does not prevents blood pressure and heart rate response to intubation.

RESPIRATORY SYSTEM

- Dose dependent decreases in ventilation is seen with doses 0.15mg/kg.
- Midazolam 0.05 -0.075mg/kg shown to depress resting ventilation.
- Transient apnea can occur.
- Also depresses swallowing reflex and decreases upper airway activity.

CENTRAL NERVOUS SYSTEM

- Decreases CMRO2, cerebral blood flow. Unlike Propofol it not produces isoelectric EEG due to its ceiling effect with respect to decrease in CMRO2 produced by increase in Midazolam doses.
- Cerebral vasomotor responsiveness to CO_2 is preserved
- Potent anticonvulsant activity
- Though it improves neurologic outcome, Benzodiazepines does not possess neuro protective activity.

DOSAGE

Sedation – 1-2.5 mg iv

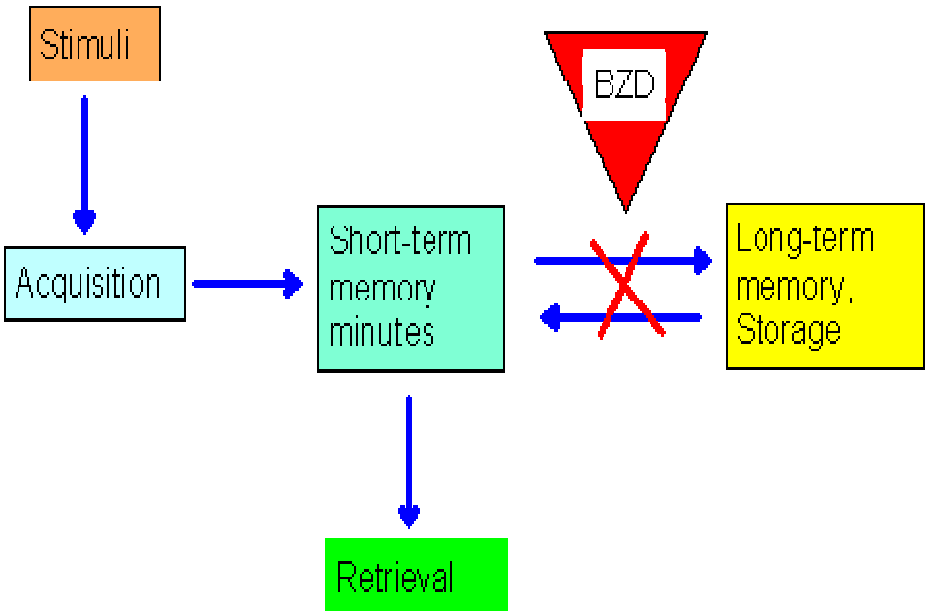
Induction – 0.1-0.5mg/kg iv

Premedication – 0.05-0.15mg/kg iv

USES

- Most commonly used benzodiazepine for premedication 0.25 - 0.5mg/kg can be used as premedication to produce anxiolysis and sedation before 20-30 minutes of anaesthetic induction.

- Anterograde amnesia



- Intravenous sedation

  Compared to Diazepam, Midazolam produces rapid onset, greater amnesia and less post operative sedation. As age increases the hypnotic effect of Midazolam increases.

- Induction of anaesthesia

  Unlike Thiopentone induction of Midazolam is slower. Along with small dose of Fentanyl ,unconsciousness is facilitated. Thus it has synergistic action with Fentanyl.

- Maintenance of anaesthesia

  Midazolam is usually administered to supplement Opioids, Propofol and inhalation agents.

- Post operative sedation

SIDE EFFECTS

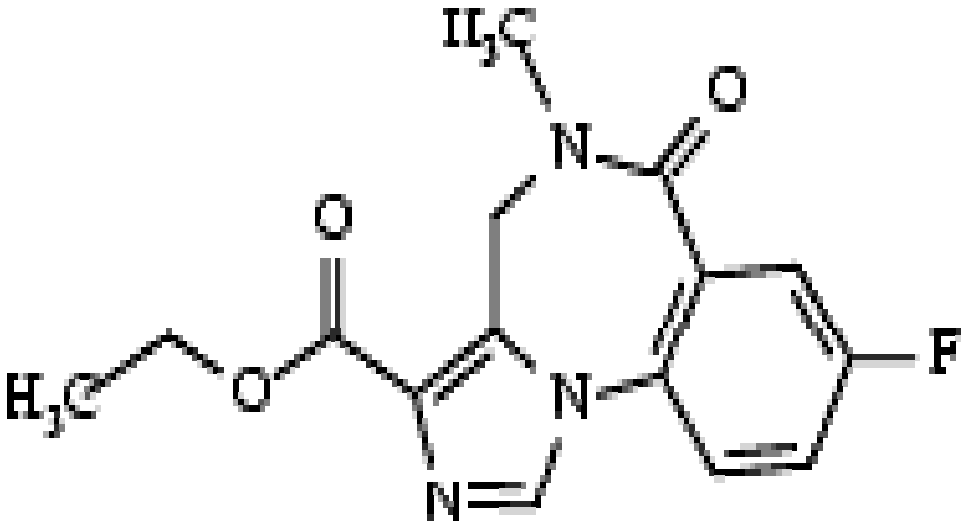
- Fatigue
- Drowsiness
- Transient anterograde amnesia
- Decreased motor co ordination and impairment of cognitive function
- Tolerance develops to drug

DRUG INTERACTIONS

- Opioid and Midazolam results in synergistic action
- Decreases MAC value of volatile anaesthetic
- Barbiturate potentiates the sedative effects

FLUMAZENIL

Benzodiazepine antagonist used to treat an overdose of Benzodiazepines



Flumazénil

- It has high affinity to Benzodiazepine receptors
- Acts as competitive antagonist
- It is given intravenously
- Plasma half life is 1 hour. Because of its short duration of action it has to be administered several times to maintain its effect.

THERAPEUTIC USES

IN INTENSIVE CARE

- For treatment of Benzodiazepine poisoning
- Differential diagnosis of state of coma of unknown origin to reveal those poisoning with Benzodiazepines

IN ANAESTHESIA

- Interruption of general anaesthesia induced and maintained by Benzodiazepines
- Interruption of sedation given by Benzodizepines
- Treatment of hepatic encephalopathy where abnormal endogenous compounds involved as Benzodiazepine agonist

INDUCTION means making the patient sleep (hypnotic state)

The term **COINDUCTION** of anaesthesia introduced in 1986.

COINDUCTION means administering a small dose of sedative or anaesthetic agent prior to induction agent to reduce the dose required for induction

AUTOCOINDUCTION is administering pre calculated dose of induction agent prior to induction with same induction agent

PROPOFOL is a suitable alternative to Thiopentone for intravenous induction of general anaesthesia. Compared to Thiopentone, induction with Propofol is smooth, rapid onset and it has got better intubating conditions due to depression of airway reflexes. And also due to blunting of baro receptor reflexes compensatory increase in heart rate does not occurs. Rapid recovery with minimal residual effects and less hang over makes Propofol a wonderful drug for induction. Even though it has all these advantages, hypotension caused by propofol induction and its cost are worrisome. To overcome these demerits COINDUCTION OR PRIMING TECHNIQUE is used in our study.

Our main aim is to improve the ratio of desired versus adverse effect of Propofol. Planned coinduction makes use of synergistic drug interactions between drugs.

By using this technique, we have undertaken this study to evaluate whether the coinduction of Propofol-Propofol or Midazolam-Propofol is better in terms of dose requirements and hemodynamic alterations compared to Propofol induction alone.

AIM OF STUDY

To compare Midazolam-Propofol coinduction with Propofol-Propofol coinduction in patients undergoing elective surgery with respect to

Primary outcome

- Total dosage of Propofol used thereby finding cost effectiveness
- Avoiding Propofol induced hypotension after induction.

Secondary outcome

- Hemodynamic alterations after intubation and 5 minutes ,10 minutes after intubation.

REVIEW OF LITERATURE

ANILKUMAR et al conducted study in 100 ASA 1 & 2 patients of both sexes between 18-55 years, scheduled for elective surgeries under general anaesthesia. All patients allocated into two groups.

GROUP 1 – CONTROL

GROUP 2 - STUDY

IN GROUP 1 patients were induced with Propofol 2mg/kg whereas patients in GROUP 2 were initially primed with 20%calculated dose of Propofol 30 seconds prior and were later induced with remaining dose of Propofol until loss of eyelash reflex.

The total induction dose requirements of Propofol and hemodynamic alterations were noted at various intervals like just before induction,one minute after induction ,immediately after intubation, five minutes after induction..

The data analysed by chi square and t test

Mean dose of Propofol used in

GROUP 1-108.12

GROUP 2-78.4

A mean reduction of 27.48% induction dose requirements of Propofol was observed in GROUP 2 (P VALUE=0.000000).

Likewise SBP,DBP,MAP found to be increased after induction (P VALUE=0.000459) in Propofol group compared to control group..

Dr ROOPAM KATERIA et al 2010 Conducted a comparative study of efficacy of Propofol autocoinduction versus Midazolam-Propofol coinduction using priming principle. 90 patients posted in upper abdominal surgery around 18-55 years of both sexes ASA 1 AND 2 where randomly allocated into three groups of 30 each

GROUP 1 - Received 0.5mg/kg iv Propofol

GROUP 2 - Received 0.05mg/kg iv Midazolam

GROUP 3 - Received 3 ml normal saline

Followed by iv induction with Propofol 2 minutes later till BIS 45 attained

The following were recorded

Total dose of Propofol required in achieving targeted BIS,HR,SBP,DBP,SPO2 just before induction, after induction, after intubation and 5 mins. Post op recall phenomenon also enquired.

They observed 31.8%reduction in induction dose of Propofol in Propofol autocoinduction group 45.37%reduction in induction dose of Propofol in Midazolam-Propofol group.($P<0.001$)

Significantly lesser fall in both SBP,DBP, in Propofol autocoinduction group at postinduction interval.

The rise in SBP,DBP after intubation was lesser in Propofol auto coinduction group($P<0.001$)

DR.UMA SRIVASTAVA et al Conducted study on smalldose of Propofol or Ketamine as an alternative to MIidazolam coinduction to Propofol.

Studied in 68 patients of ASA 1 AND 2 of both sexes,aged 20-40 years undergoing general,orthopaedic surgery were randomly allocated into 4 groups

GROUP KP- received 0.3mg/kg Ketamine

GROUP MP-received 0.03 mg/kg Midazolam

GROUP PP- received 0.4 mg/kg Propofol

GROUP SP- received 3 ml normal saline

Followed by Propofol induction till loss of verbal commands.

Dose required to induce anaesthesia was significantly lesser in

GROUP KP-1.2 mg/kg

GROUP MP-1.4mg/kg

GROUP PP -1.6mg/kg

Than CONTROL GROUP 2.7mg/kg

Fall in BP was maximal in Control group, and it was least in Ketamine group.

DR MINAXI H SHAH et al Conducted study on comparison of Midazolam-Propofol coinduction with Propofol predosing for induction of anaesthesia

Studied in 90 patients of ASA1 AND 2 aged 17-60 years of both sexes for elective day care surgery

GROUP 1 - Control

GROUP 2 - Received Midazolam 2mg iv

GROUP 3 - Received Propofol 30mg iv

Then induced with Propofol using loss of verbal command.

They found in

GROUP 2 -38.26%

GROUP 3- 36.10%

Reduction in Propofol usage compared to Control group.

Midazolam coinduction is more economical than Propofol predosing and also an effective method for reducing pain on injection with Propofol.

Dr DJAIANIG & RIBES et al Studied in 54 undergoing day care anaesthesia for minor orthopaedic surgery.

GROUP 1-Midazolam 0.05 mg/kg iv

GROUP 2-Propofol 0.4mg/kg

GROUP 3- Normal Saline

Followed 2 minutes later by Propofol infusion at a rate of 50mg/kg/hr until loss of eyelash reflex. Compared pre and post induction hemodynamic changes, complications at insertion of LMA and recovery.

They found in both GROUP 1 AND 2 reduction in Propofol usage compared to control GROUP 3.

LEONG et al Studied Propofol auto coinduction can aid LMA insertion

44 ASA 1 AND 2 patients scheduled for surgery were randomly allocated into 2 groups.

GROUP 1-Propofol 0.5 mg/kg

GROUP 2-Normal saline

Then Propofol infusion started at 50 mg/kg/hr till loss of eyelash reflex Observed significant difference in group 1 in requirement of Propofol.

N.A.JONES, S.ELLIOT et al compared induction of anaesthesia in elderly patients with Midazolam-Propofol coinduction and Propofol predosing.

They selected 60 patients of both sexes aged more than 70 years posted for urological surgery.60 patients divided to 20 each of three groups.

GROUP 1- Midazolam 0.02mg/kg iv given

GROUP 2-Propofol 0.25mg/kg iv given

GROUP 3-Normal saline 2ml iv given

After 2 minutes all these groups were induced with Propofol 1%infusion 300ml/hr. End point of induction was taken as loss of response to verbal command and placement of oropharyngeal airway.

Cardiovascular response monitored at 1 minute interval until induction was complete.

They observed Group 1(Midazolam-Propofol) had lesser requirement of Propofol than Group 3(placebo) P value=0.05,which shows it s significant

There was no significant difference in dosage of Propofol used while comparing Group 1 (Propofol group) with Group 3(placebo).

There was no demonstrable difference in terms of cardiovascular stability between three groups.

DR MOHRIN NAZIR BUTT et al Compared Ketamine –Propofol and Midazolam-Propofol coinduction.

Their primary outcome was the dose of Propofol required in two groups. They selected 60 patients of both sexes aged 20-50 years belonged to ASA 1 & 2 undergoing day care surgery.

GROUP K – Ketamine 0.3mg/kg iv

GROUP M – Midazolam0.03 mg/kg iv

Followed by 2 minutes after induction with Propofol 10mg/5secs until patient stopped counting numbers and loss of verbal commands.

They found mean induction dose between groups is not significant.

GROUP K-53.67

GROUP M-52.33

P=0.78 Not significant

DR GOJENDRA RAJKUMAR,RUPENDRA THOKCHAM et al

Compared coinduction of Midazolam, Thiopentone, Ketamine with Propofol in general anaesthesia. 120 patients posted for general and gynaecological surgery were allotted in 4 groups of 30 each.

GROUP 1 –Normal saline 2 ml

GROUP 2 – Midazolam 0.03 mg/kg

GROUP 3 – Thiopentone 1 mg/kg

GROUP 4 – Ketamine 0.3mg/kg

After 2 minutes all these groups were induced with Propofol 30mg/10 secs until loss of response to oral commands or loss of eyelash reflex. Total induction dose of Propofol required and parameters like HR, SBP, DBP, MAP were monitored.

Total induction dose requirements was decreased in group 2,3,4 compared to control group 1.

GROUP 2 -33.92%

GROUP 3-35.08%

GROUP 4-42.69%

They observed fall in MAP from baseline in all the groups.

GROUP 2-10.8%

GROUP 3-14.58%

GROUP4-8.37%

They observed Ketamine reduced the induction dose requirements more compared with the other groups.

All three study groups provided hemodynamic stability but Ketamine group proved to be better than the other two study groups.

YOUNG SOO LIM et al studied the Cardiovascular effects of Midazolam coinduction to Propofol for induction of general anaesthesia in elderly patients.

They conducted in 80 patients of more than 65 years undergoing general surgery.

GROUP 1 – 0.9%Nacl 0.03 ml/kg ,Propofol 1.2mg/kg,Remifentanyl

GROUP 2 – Midazolam 0.03mg/kg,Propofol 0.8mg/kg ,Remifentanyl

Time taken for loss of consciousness and BIS at loss of consciousness were recorded. After loss of consciousness 0.8mg/kg of Rocuronium was given. All vital parameters noted.

MBP at before intubation and 3 minutes after intubation was significantly reduced in both groups. Compared with Group 1,the decrease in MBP was less in Group 2.($p=0.05$)

Time taken to reach loss of consciousness was significantly reduced in Group 2 compared with Group1.($p<0.05$)

No significant difference in heart rate at any time between groups.

They concluded the study as, coinduction prevent a marked reduction in blood pressure at induction and after intubation in aged patients.

MARTLEW RA MEAKING G et al conducted a study in children of age groups 3-12 years undergoing general anaesthesia for minor surgery to evaluate Midazolam premedication to Propofol induction .

100 patients of two groups.

GROUP 1- No premedication

GROUP 2 –Oral Midazolam 0.5mg/kg 30 to 60 minutes before anaesthesia.

Both groups were induced with Propofol iv over 15 seconds. Condition for LMA insertion assessed. Vitals and total dose requirements observed.

Dose response curve were parallel in Group 1 (not pre medicated) but in Group 2 (pre medicated) shifted to left of not pre medicated curve.

Propofol requirements also decreased by one third in pre medicated group compared to not pre medicated group.(p=0.0001)

Dose required for LMA insertion in Group 1-3.8mg/kg

Group 2-2.6 mg/kg

They concluded that Midazolam premedication to Propofol was better in children undergoing surgery.

DRIVER IK ,WILTSIRE S et al did a randomised trial on sedative premedication before Propofol induction.

Conducted study on 90 un premedicated patients undergoing elective gynaecological studies.90 patients were divided to three groups of 30 each.

GROUP P - Propofol only 2.5mg/kg

GROUP PA - Alfentanyl 10mic/kg 90 seconds prior to Induction with Propofol 1.25mg/kg

GROUP PMA- Midazolam 0.04 mg/kg 3 minutes, Alfentanyl 10 mic/kg 90 seconds prior to Propofol induction of 1.25 mg/kg

The end point of induction was taken as loss of response to verbal commands or eye lash reflex. If inadequate 0.25mg/kg every15 seconds was given.

Vital signs like HR,SBP,DBP, mouth opening graded.

They observed Group PMA requires less Propofol consumption than other two groups($p<0.001$).

Group PMA had better mouth opening than other groups.

GOEL S BHARDWAJN et al did a randomised trial on Ketamine, Midazolam coinduction with Propofol in general anaesthesia. Conducted in 60 children of age group 1-8 years. Alloted 3groups of 20 each.

GROUP P- Normal saline followed by Propofol 3.5mg/kg

GROUP PK- Ketamine 0.5mg/kg followed Propofol 2.5mg/kg

GROUP PM-Midazolam 0.05mg/kg followed by Propofol 2.5mg/kg

And LMA inserted 30 seconds later. Vital signs were monitored.

Group PK and Group PM found to be better than Group P with respect to LMA insertion.($p<0.05$).

There was fall in blood pressure in all three groups. Only 5% of patients in Group PK and Group PM showed more than 20% fall in SBP, where as 89% of patients showed more than 20% fall in SBP.($P<0.0005$)

They concluded that Ketamine and Midazolam coinduction with Propofol had better hemodynamic stability than induction with Propofol alone. Though they had better hemodynamics they were associated with delayed recovery.

DR W M LEONG et al Conducted study on Propofol auto coinduction aid LMA insertion. They did in 44 patients in two groups undergoing general or orthopaedic surgery.

GROUP PP-0.5 mg/kg Propofol 2 minutes prior to induction

GROUP CP-2 ml normal saline 2 minutes prior to induction

Followed by 50mg/kg/hr till loss of eyelash reflex.

They compared time taken for induction and LMA insertion, total dose of Propofol needed,hemodynamics.

Significant reduction in dose was seen in Group PP than Group CP.

GROUP PP-100

GROUP CP-166 (P=0.0001)

Jaw opening was ease with Group PP

Significant reduction in MAP in each group seen after induction. But the magnitude of decrease in each group was not significant between groups.

Thus they concluded Propofol autocoinduction was better in LMA insertion than inducing with Propofol alone.

DONALD C OXAN et al studied the effects of Midazolam on Propofol induced anaesthesia withrespect to Propofol dose requirements,mood profiles and perioperative dreams.

They conducted in females undergoing dilatation and curettage surgery.60 patients of 30 each in two groups were allotted.

GROUP 1 – Midazolam 30 mic/kg

GROUP 2- Placebo

Followed by induction with Propofol. Loss of verbal contact was taken as end point of induction. Vitals monitored.

They didn't find any significant difference in dose of Propofol required to induce hypnosis or maintain anaesthesia.

Dr DIMPLE WALLY et al compared Propofol predosing with Midazolam coinduction in LMA insertion.

Conducted on 60 patients in three groups of 20 each

GROUP 1 – Normal saline

GROUP 2 – Midazolam

GROUP 3 - Propofol

All three groups were followed by Propofol induction. Vitals were monitored.

HR, SBP, DBP, MAP were decreased in all three groups.

Induction dose in Group 2-106.3

Group 3-136.5

Group 1-159.75

No statistical difference observed between Group 2 and Group 3 with respect to dose of Propofol required. But was significant when compared with control group.

They concluded that Midazolam coinduction and Propofol auto coinduction were safe alternative to induction of Propofol alone.

With respect to cost effectiveness Midazolam coinduction was more economical and better than Propofol coinduction.

ANDERSON H ROBB et al studied the comparison of Midazolam coinduction with Propofol predosing for induction of general anaesthesia .

Conducted on 90 patients of ASA 1&2 of both sexes. Divided into three groups of 30 each.

GROUP 1- Midazolam 2 mg

GROUP 2-Propofol 30 mg

GROUP 3- placebo

Followed by Propofol induction till loss of verbal contact and tolerance to placement of facemask.

Requirement of Propofol in Group 1-1.71mg/kg

Group 2-1.87mg/kg

Group 3-2.38m/kg

Predosing decreases Propofol usage in both study groups compared to control group. They observed no significant difference in hemodynamics.

J.A LEITCH, ANDERSON at al conducted randomised trial on patients maintained in Propofol sedation &operator controlled Midazolam sedation in third molar extraction

Two groups were compared before, during and after sedation.

1. Their primary outcome were time until discharge
2. Oxygen saturation

Vital signs, anxiety, psychomotor skills were also compared.

Anxiety decreased greater in Propofol group(P=0.010)

Propofol group recovered quicker (P=0.010). Smaller decrease in saturation($p<0.001$).smaller decrease in heart rate($p<0.001$)

Thus Propofol produces superior anxiolysis, quicker recovery, less amnesia, less depression of psychomotor function.

NI NI WIN KCHASE et al Conducted trial on hemodynamic changes during Midazolam Propofol coinduction. Conducted in 40 patients of 20 each in two groups.

GROUP 1 – Propofol 2.5mg/kg

GROUP 2 –Midazolam 0.1mg/kg followed by Propofol 1.5 mg/kg

Parameters like LF(low frequency component) which reflects both cardiac sympathetic and parasympathetic activity.

HF (high frequency component) which reflects cardiac parasympathetic activity

TOTAL POWER calculated by LF+HF and LF/HF RATIO which reflects balance between cardiac sympathetic and parasympathetic activity.

In Group 2- significant increase in LF/HF ratio observed before intubation, after intubation.

Thus Midazolam Propofol coinduction is better in preserving hemodynamics reduction in dose and time taken for LMA insertion in Propofol group.

MATERIALS AND METHODS

This study was approved by our Institutional Ethics Committee, and it was conducted in our Institute of anaesthesiology and critical care. Madras Medical College, Rajiv Gandhi general hospital, Chennai. The study was a Prospective, Randomised controlled study.

This study was conducted on 90 patients of ASA 1 & 2 of both sexes undergoing elective surgery

INCLUSION CRITERIA

- Age : 18 – 60 years
- ASA : 1 & 2
- Weight : 40 – 80 kg
- Surgery :elective
- Who have given valid informed consent

EXCLUSION CRITERIA

- Not satisfying inclusion criteria
- Lack of written informed consent
- Patients undergoing Emergency surgery
- Pregnant females
- Difficult airway
- Allergic to medications

MATERIALS

- Drugs – inj Glycopyrrolate, inj Fentanyl, inj Midazolam,inj Propofol, inj Succinylcholine, Non depolarising muscle relaxants, volatile agents, all other emergency drugs
- Laryngoscope with different size blades, bougie, airways
- Different sizes of endotracheal tubes
- Monitors – ECG, NIBP ,SPO2
- Suction apparatus

METHODS

The patients who satisfied the above inclusion criteria were included in this study after getting a valid informed consent from them.

The three groups were randomised by lot system into

GROUP 1 - Received normal saline 2 ml

GROUP 2 - Received Midazolam 0.05 mg/kg iv

GROUP 3 - Received Propofol 0.5 mg/kg iv

All this group then induced with Propofol 2 minutes later. The end point of induction is taken as loss of response to verbal commands.

PREOPERATIVE

Age, weight, comorbid conditions, any history of previous surgery, vitals like pulse rate, blood pressure,spo2,baseline investigations like haemoglobin, blood sugar, blood urea, serum creatinine, serum electrolytes, ECG, Chest X ray were checked. Thorough systemic examination and airway examination were done and patients were selected in this study and allocated into groups.

INTRAOPERATIVE

90 patients of age group 18-60 years of both sexes belonging to ASA 1&2 posted for elective surgery were allocated into 3 groups of 30 each by lot system.

Patients were shifted to operating room as scheduled. Monitors were connected and baseline parameters like heart rate, blood pressure,spo2 were recorded. Baseline value recorded as an average of three readings taken 5 minutes apart before 10 minutes of starting the general anaesthesia. Patients were given Inj. Glycopyrrolate 10 mic/kg iv, Inj .Fentanyl 2 mic/kg iv ten minutes before starting and pre oxygenated with 100% oxygen.

Then according to group stratification

GROUP 1 - Received normal saline 2ml

GROUP 2 - Received Midazolam 0.05 mg/kg iv

GROUP 3 - Received Propofol 0.5 mg/kg iv

After two minutes patients of all three groups are induced with Propofol till loss of response to verbal command as end point. Propofol induced at a rate of 10 mg/10secs. This speed is kept constant in all three groups. After loss of response to verbal commands anatomical mask was kept over the patient face, if there was any resistance on keeping mask over face additional bolus of 10 mg given till there was no disturbance in holding mask. Complications like apnea, laryngospasm, vomiting, coughing are noted.

Then the patients were given muscle relaxant Succinylcholine 2 mg/kg iv and intubated with appropriate size endotracheal tube and ventilation was controlled. Anaesthesia was maintained by using O_2 : N_2O (33:66) and volatiles like sevoflurane, desflurane. Non depolarising muscle relaxant like Atracurium used as muscle relaxant intraoperatively. Surgery started after 10 mins. During this period no stimuli applied to patient.

Parameters like Heart rate, systolic blood pressure, diastolic blood pressure, oxygen saturation were recorded just before induction, after induction, after intubation, after 5 minutes and 10 minutes of intubation.

Total dose of Propofol used also noted.

After procedure patients are extubated and sent to post operative wards.

PRIMARY OUTCOME MEASURES

- Total dose of Propofol needed
- Hemodynamic alterations just before induction, after induction

SECONDARY OUTCOME MEASURES

- Hemodynamic alterations after intubation, 5minutes and 10minutes after intubation.

STATISTICAL ANALYSIS

Statistical analysis was done using statistical package for social sciences windows version 15.Results expressed in this study were given as mean and standard deviation.

All continuous variables like age, weight, HR, SBP, DBP, MAP were compared using ANOVA (ANALYSIS OF VARIANCE)

Chi square test used to compare between sex and ASA

P value <0.05 was considered significant

OBSERVATION AND RESULTS

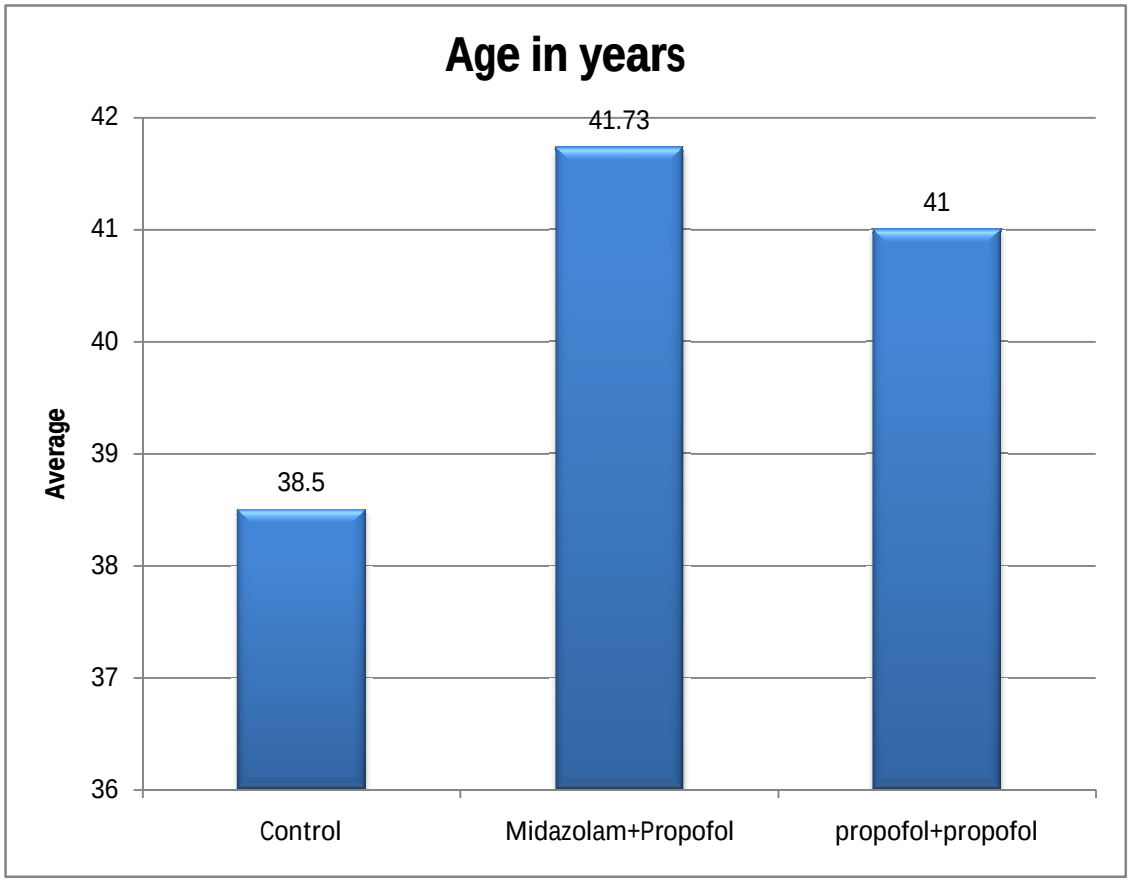
DEMOGRAPHIC DATA

The three groups were compared with respect to age, sex, weight and ASA physical status. The results were discussed as follows:

TABLE – 1: AGE DISTRIBUTION

GROUPS	N	Mean	Std. Deviation	ANOVA F value	P value	Significance
Control	30	38.50	11.557	.471	.626	NS
Midazolam-Propofol	30	41.73	13.903			
Propofol-Propofol	30	41.00	14.923			

GRAPHICAL REPRESENTATION OF AGE GROUPS

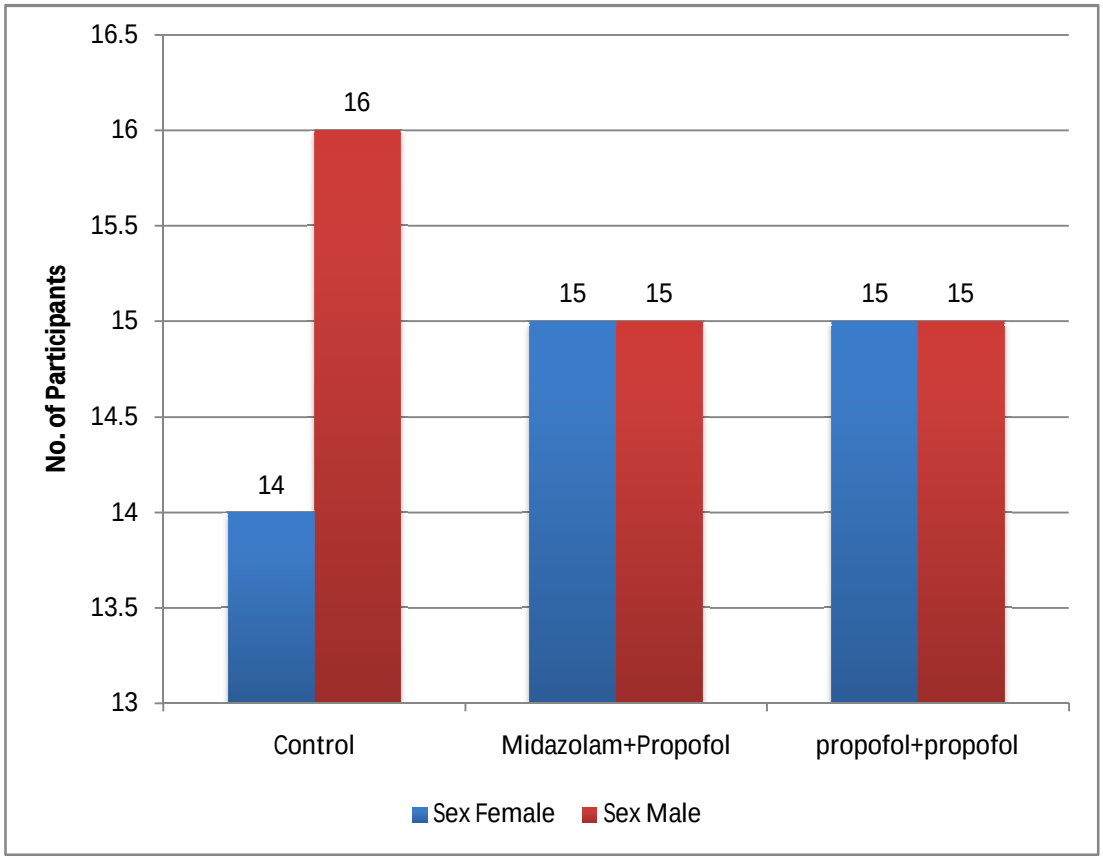


P VALUE of 0.626 derived for age distribution among three groups, which is not statistically significant. This shows we have compared similar age group patient.

TABLE – 2 : SEX DISTRIBUTION

SEX	Group						
	Control		Midazolam-Propofol		Propofol-Propofol		Chi-square
	N	%	N	%	N	%	
Female	14	46.7%	15	50.0%	15	50.0%	0.089, P>0.05 NS
Male	16	53.3%	15	50.0%	15	50.0%	

GRAPHICAL REPRESENTATION OF SEX DISTRIBUTION

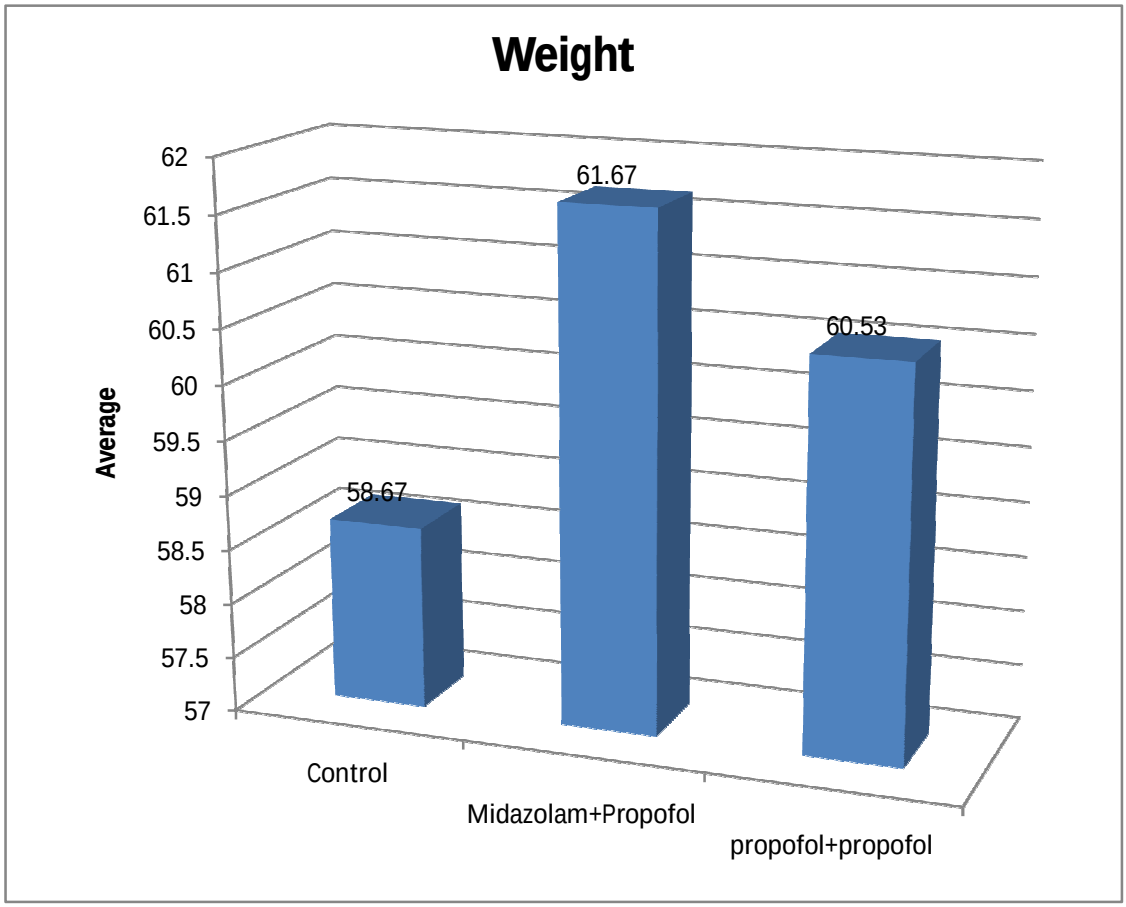


P value of 0.089 derived among three groups, which showed no significant difference between groups. It shows we have compared similar sex between groups.

TABLE – 3: WEIGHT DISTRIBUTION

Group	N	Mean	Std. Deviation	ANOVA F value	P value	Significance
Control	30	58.67	7.189	.978	.380	NS
Midazolam+Propofol	30	61.67	8.999			
Propofol+Propofol	30	60.53	8.862			

GRAPHICAL REPRESENTATION OF WEIGHT DISTRIBUTION



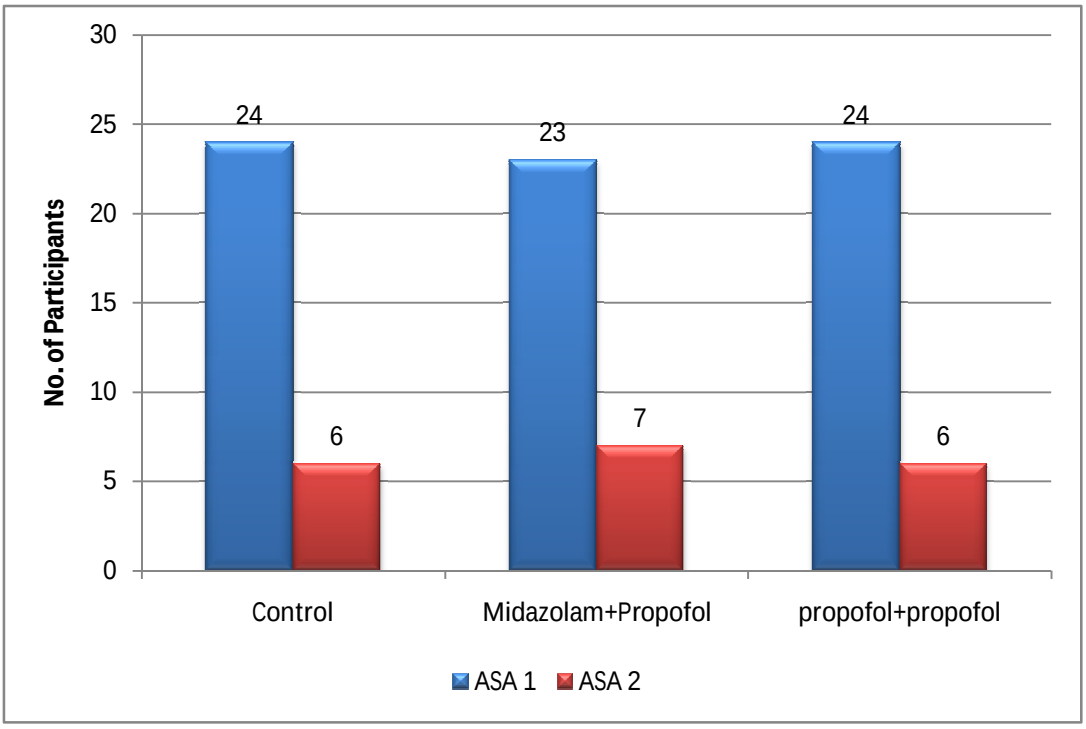
We got P value of 0.380 in weight distribution among three groups, which is not significant between groups.

This showed we compared three groups of similar weight patients.

TABLE – 4 : ASA STATUS OF GROUPS

ASA	Group						Chi-square
	Control		Midazolam-Propofol		Propofol-Propofol		
	N	%	N	%	N	%	
1	24	80.0%	23	76.7%	24	80.0%	0.133
2	6	20.0%	7	23.3%	6	20.0%	P>0.05 NS

GRAPHICAL REPRESENTATION OF ASA STATUS

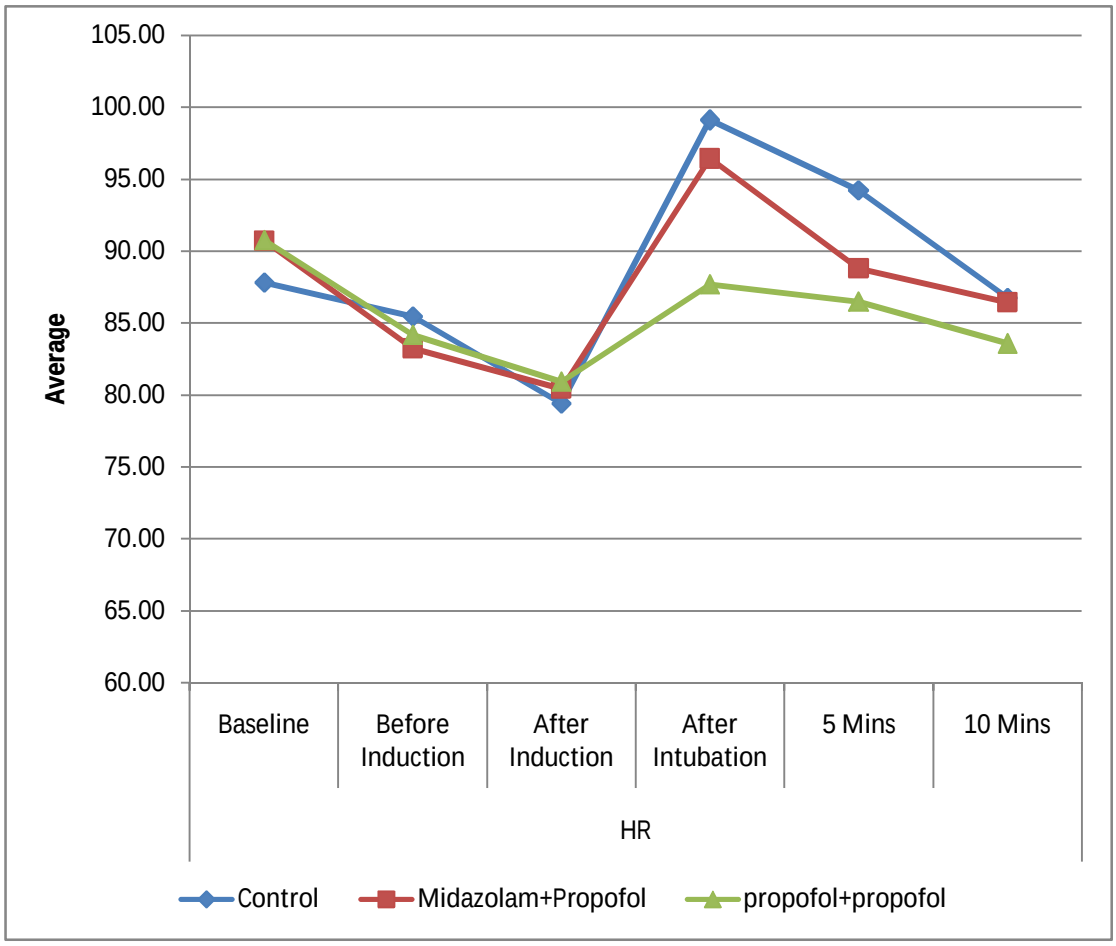


With respect to ASA status, we didn't find any significant difference between three groups. We got P value of 0.13 which showed no significance in groups.

TABLE – 5: HEART RATE VARIATIONS

HR	Control		Midazolam-Propofol		Propofol-Propofol		F	P value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	87.83	13.42	90.70	13.58	90.77	16.18	.403	.669
Before Induction	85.47	12.80	83.23	10.96	84.17	14.74	.226	.798
After Induction	79.40	12.16	80.43	10.29	80.93	12.33	.136	.873
After Intubation	99.10	12.86	96.43	10.93	87.70	14.43	6.491	.002*
5 Mins	94.23	11.05	88.80	8.50	86.47	13.26	3.862	.025*
10 Mins	86.73	10.04	86.43	9.66	83.57	11.65	.834	.438

GRAPHICAL REPRESENTATION OF HEART RATE



There was no significant changes in heart rate variation between three groups in recordings taken just before induction, after induction, 10 minutes after intubation.

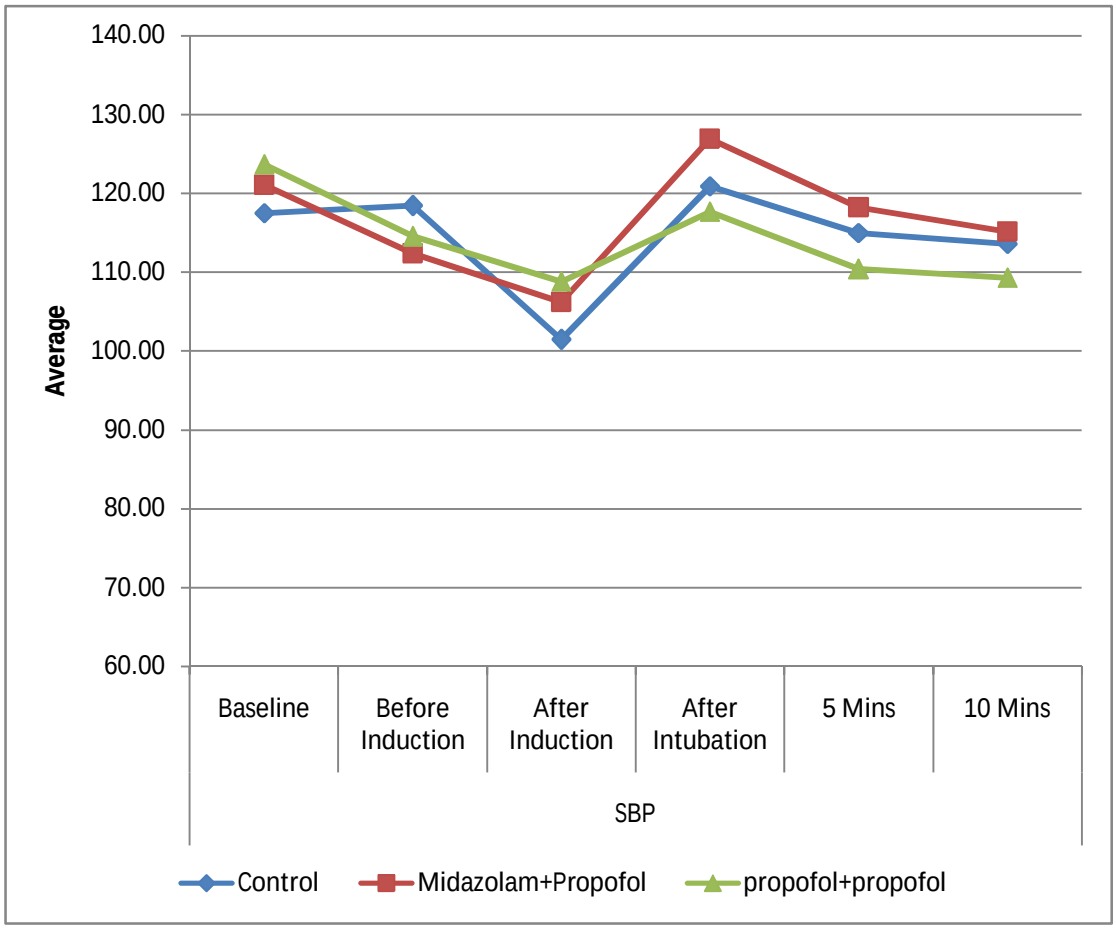
Heart rate variations was found to be significant in recordings taken after intubation, 5 minutes after intubation among three groups.

Increase in heart rate after intubation was greater in control group, and found to be least in Propofol group. (p=0.002)

TABLE 6 : VARIATIONS IN SYSTOLIC BLOOD PRESSURE

SBP	Control		Midazolam +Propofol		Propofol +Propofol		F	P value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	117.53	9.85	121.07	11.10	123.70	10.00	2.691	.073
Before Induction	118.43	9.63	112.40	10.12	114.53	9.19	3.012	.054
After Induction	101.47	10.05	106.23	10.59	108.80	9.47	4.115	.020*
After Intubation	120.93	12.81	126.93	9.94	117.67	12.18	4.833	.010*
5 Mins	115.00	9.64	118.20	11.29	110.40	12.47	3.682	.029*
10 Mins	113.60	9.21	115.13	8.48	109.33	10.31	3.092	.050

GRAPHICAL REPRESENTATION OF SYSTOLIC BLOOD PRESSURE



We found significant difference in readings taken after induction, after intubation, 5 minutes after intubation among three groups. There was no significant difference seen 10 minutes after intubation.

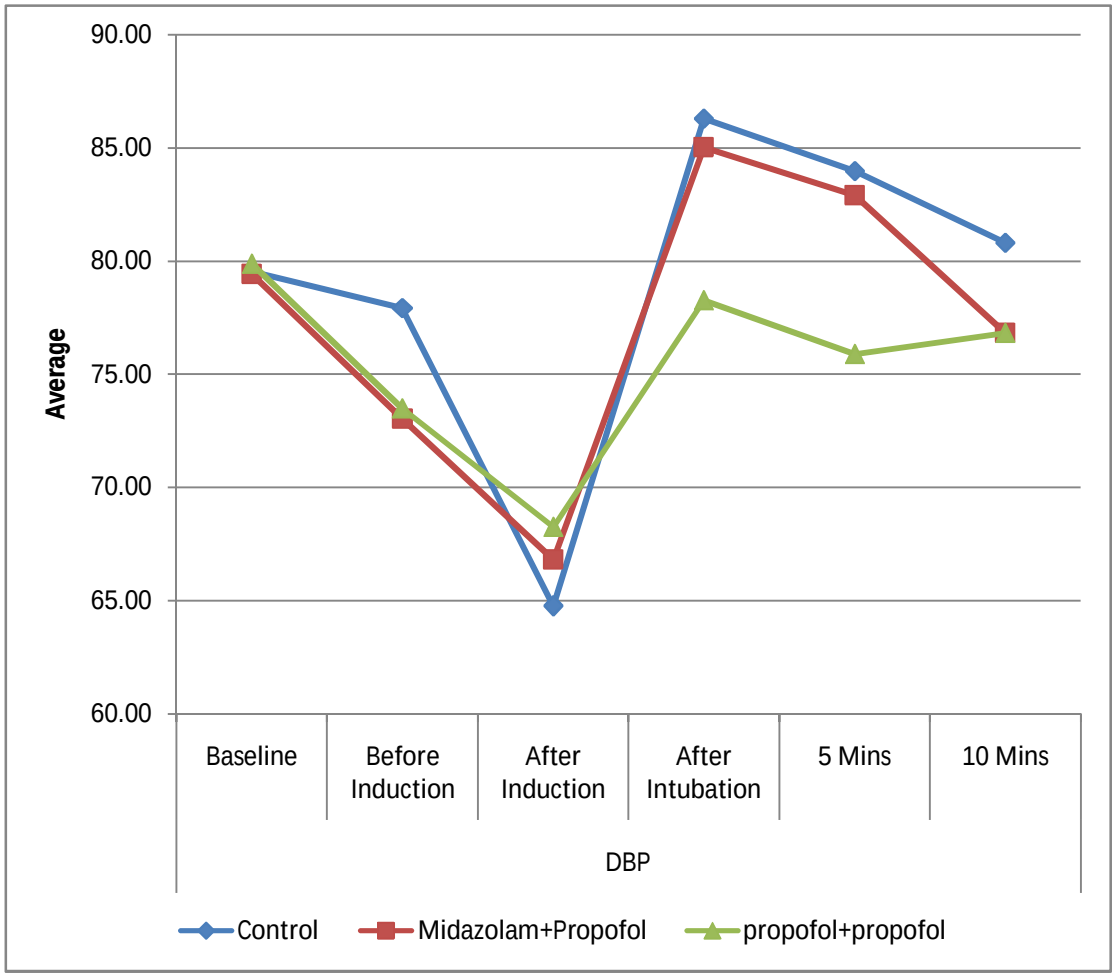
In our study SBP after induction falls greater in control group, and it was least in Propofol-Propofol group (p =0.020).

SBP after intubation was greater in control group and it was least in Propofol-Propofol group (p=0.010).

TABLE 7: VARIATIONS IN DIASTOLIC BLOOD PRESSURE

DBP	Control		Midazolam +Propofol		Propofol +Propofol		F	P value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	79.53	8.72	79.43	7.01	79.87	5.66	.029	.971
Before Induction	77.93	8.23	73.03	7.08	73.50	7.73	3.706	.029*
After Induction	64.77	9.60	66.83	7.94	68.27	7.24	1.342	.267
After Intubation	86.30	6.11	85.03	4.76	78.27	6.94	15.520	P<0.01*
5 Mins	83.97	6.87	82.90	6.79	75.90	5.24	14.309	P<0.01*
10 Mins	80.80	7.36	76.83	6.27	76.83	6.77	3.387	.038*

GRAPHICAL REPRESENTATION OF DBP VARIATIONS

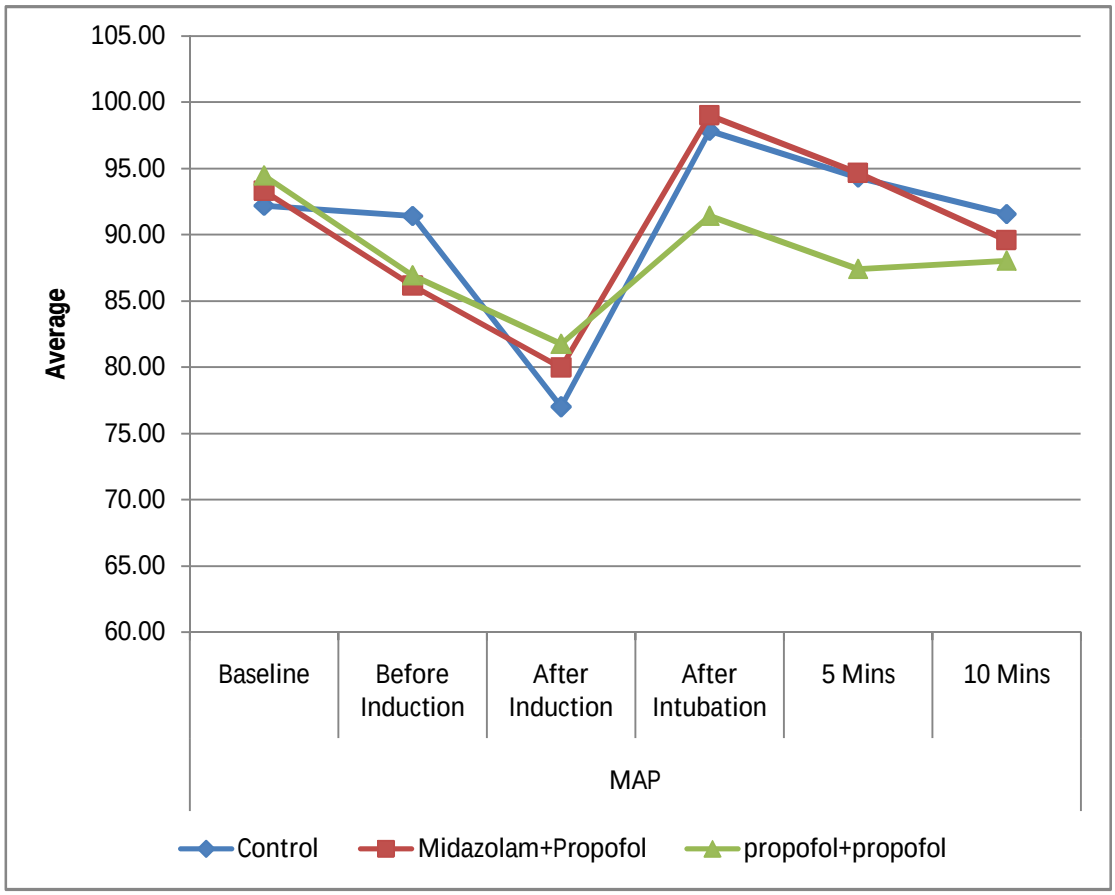


We found variations of diastolic blood pressure are significant between three groups in readings noted in after intubation, 5 minutes after intubation. There was greater rise in DBP seen after intubation in control group, and it was least in Propofol-Propofol group(p=<0.01). There was no difference seen 10 minutes after intubation.

TABLE 8 : VARIATIONS IN MEAN BLOOD PRESSURE

MAP	Control		Midazolam-Propofol		Propofol-Propofol		F	P value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	92.20	8.79	93.31	7.71	94.48	6.47	.653	.523
Before Induction	91.43	8.40	86.16	7.08	86.92	6.68	4.431	.015*
After Induction	77.00	9.31	79.97	7.69	82.24	5.99	3.425	0.037*
After Intubation	97.84	7.57	99.00	5.58	91.40	8.06	9.836	P<0.01*
5 Mins	94.31	7.05	94.67	6.58	87.40	6.62	11.030	P<0.01*
10 Mins	91.56	6.49	89.60	5.56	88.02	7.14	2.274	.109

GRAPHICAL REPRESENTATION OF TRENDS IN MAP



Mean arterial blood pressure was found to be significant in recordings noted on after induction, after intubation, 5 minutes after intubation. There was no difference noted after 10 minutes of intubation.

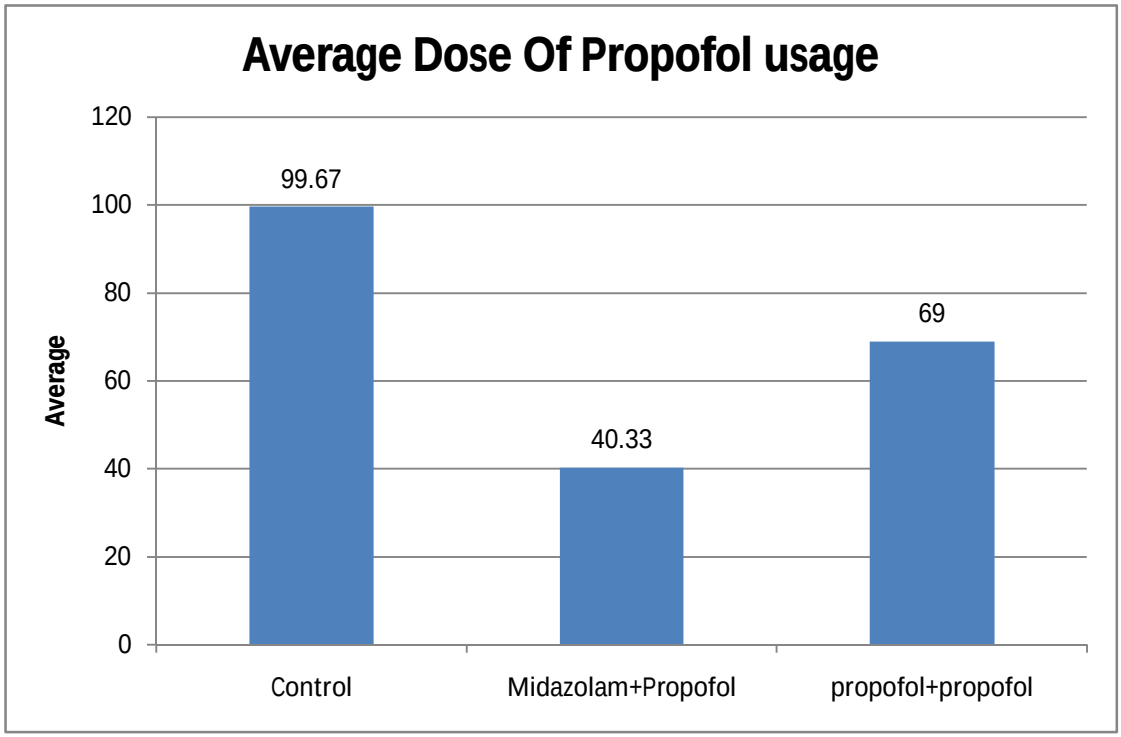
After induction MAP was greater in Propofol-Propofol group, and it was least in control group ($p=0.037$).

After intubation MAP variations showed significant difference between the groups.MAP was greater in control group, and it was least in Propofol-Propofol group ($p<0.01$).

TABLE 9 : TOTAL DOSE OF PROPOFOL USED

GROUP	N	Mean	SD	ANOVA F value	P value	Significance
Control	30	99.67	9.994	228.350	P<0.001	S
Midazolam-Propofol	30	40.33	9.279			
Propofol-Propofol	30	69.00	12.690			

GRAPHICAL REPRESENTATION OF TOTAL PROPOFOL USED



There was significant reduction in usage of Propofol among three groups. We found greater reduction in Midazolam-Propofol group ($p<0.001$).

DISCUSSION

In this study on 90 patients of 30 each in three groups we were comparing the Midazolam-Propofol group and Propofol-Propofol group in terms of total dose requirements of induction agent Propofol and hemodynamics after induction, hemodynamics after intubation and hemodynamics after 5 & 10 minutes of intubation with control group.

HEART RATE

On comparing the heart rate between groups, there was no significant difference in heart rate after induction.

After intubation heart rate is increased in all three groups.

- In control Group – 99.10
- In Midazolam-Propofol Group-96.43
- In Propofol-Propofol Group-87.70

Heart rate was increased maximum in control group compared to other two groups.

Heart rate was increased greater in Midazolam–Propofol group compared to Propofol-Propofol group. Thus there was significance in heart rate variations after intubation. (P value =0.002) There was no difference seen after 10 minutes of intubation.

Similar results was obtained by Kataria et al[19] studies where heart rate increased in all three groups with least in Propofol auto coinduction group after intubation. They also noted significant fall in heart rate in Propofol group in post priming period.

This observation may be due to the reason that Midazolam does not prevent increase in heart rate that occurs due to intubation. Unlike Thiopentone Propofol prevents compensatory increase in heart rate due to blunting of baroreceptor reflex.

MEAN SYSTOLIC BLOOD PRESSURE

In our study **Mean SBP falls after induction** in all three groups.

- In control group from 118 to 101
- In Midazolam-Propofol group from 112 to 106
- In Propofol-Propofol group from114 to 108

In our study P value of 0.020 obtained which shows significant difference between groups. There was fall in Systolic blood pressure after induction which was greater in control group and was least in other two groups.

Mean Systolic blood pressure was **increased** after intubation, 5 minutes after intubation in all three groups.

- In control group-120.93
- In Midazolam –Propofol group-126.93
- In Propofol-Propofol group-117.67

P=0.010 showed significant difference between groups.

There was greater rise in control group compared to Propofol–Propofol group after intubation. We found greater rise in mean systolic blood pressure in Midazolam-Propofol group compared to Propofol- Propofol group after intubation.

In studies by ANILKUMAR[20] et el Mean SBP in Propofol auto coinduction group was higher after induction (p=0.000002) after intubation (p=0.00000) 5minutes (p=0.00000)

In a study by KATERIA[19] et al Mean SBP falls in all groups. 20%increase in Mean SBP obtained in Midazolam group after intubation.

In a study conducted by GOEL S BHARDWAJAN[29] et al SBP falls >20% in 80%of control group compared to only 5% in Propofol Ketamine group.

In studies by YOUNG SOO LIM[26] fall in SBP was lesser in Midazolam-Propofol compared with control group.

MEAN DIASTOLIC BLOOD PRESSURE

In our study **Mean Diastolic blood pressure** showed no significant difference between groups before induction, after induction.

After intubation there was significant difference in Diastolic blood pressure ($P<0.01$).

- In control group-86.30.
- In Midazolam-Propofol group-85.03
- In Propofol-Propofol group-78.27

Mean diastolic blood pressure increased in all three groups after intubation. It was found least in Propofol-Propofol group.

In a study by DJAIANI[22] et al DBP was higher in Propofol coinduction group after induction and after intubation.

MEAN ARTERIAL BLOOD PRESSURE

In our study MAP found to be significant between groups.

Compared to control group, Propofol-Propofol group had least fall in MAP after induction and least rise in MAP after intubation.

- After induction Control Group -77.00

  Propofol-Propofol group-82.24

- After intubation Control Group-97.84

  Propofol-Propofol Group-91.40

Compared with Midazolam-Propofol group, Propofol- Propofol group had least rise in MAP after intubation.

- Midazolam- Propofol Group-99.00
- Propofol-Propofol Group-91.40

In studies by UMA SRIVASTAVA[4] et al after induction MAP significantly falls in all three groups. Here 21%decrease was seen in control which is more than other groups.4% in Ketamine group which is least. No difference existed between Propofol and Midazolam group.

In studies by GOJENDRA RAJKUMAR[25] et al fall in MAP from baseline was10.8% in Midazolam group.8.37% in Ketamine group compared to control group.

In studies by YOUNG SOO LIM[26] et al MAP decreased before intubation and 3 minutes after intubation both in conrol group and Midazolam group. Decrease in MAP was lesser in Midazolam group ($P<0.05$).

In studies by WM Leong[30] et al MAP decreased in both control and Propofol auto coinduction group but magnitude of decrease is same in both the groups.

Fall in blood pressure in Propofol is due to inhibition of vasomotor activity with loss of vasomotor tone and due to decrease ionotropic effect. Hypotension exaggerated when given in large doses, rapid injection. So we might found greater fall in blood pressure in control group compared to Propofol-Propofol group due to larger usage of Propofol in control group.

Midazolam also decreases blood pressure by reducing total peripheral resistance. So compared to Propofol-Propofol group there was fall in blood pressure in Midazolam-Propofol group.

TOTAL DOSE OF PROPOFOL

In our study total dose of Propofol used was

- In control group-99.67
- In Midazolam-Propofol group-40.33
- In Propofol-Propofol group-69.0

This Showed significant difference in Propofol requirements.($p<0.001$) between groups.

There was greater requirement of Propofol in control group compared to other groups. Propofol usage was greater in Propofol-Propofol group compared to Midazolam –Propofol group.

This observation might be due to prior administration of sedative results in anxiolysis which reduces sympathetic drive and therefore reduces the induction dose to produce hypnosis. The synergistic effect of Midazolam and Propofol was responsible in least usage of Propofol for induction while using their coinduction technique.

In a study by KATERIA[19] et al they found 31.88% reduction in Propofol usage in Propofol autocoinduction.45.37%reduction in Midazolam-Propofol coinduction.

In studies by ANILKUMAR[20] et al they found 27.88% reduction in Propofol auto coinduction.

In studies by UMA SRIVASTAVA[4] et al they obtained reduction of 40% in Midazolam coinduction and 48% in Propofol autocoinduction

In studies by MINAXI[21] et al 38.26%reduction in Midazolam group and 36.10%in Propofol coinduction group.

In studies by MARTLEW RA[28] et al Propofol requirement decreased by one third $P<0.0001$.Dose required for LMA insertion in not premedicated group was 3.8mg/kg and in premedicated children 2.6mg/kg

In studies by ANDERSON H ROBB[7] et al dosage requirements for control was 2.38 mg/kg .In Propofol autocoinduction 1.87 mg/kg , In Midazolam –Propofol coinduction 1.87mg/kg

Thus in our study we observed reduction in total dose of Propofol was greater in Midazolam-Propofol group. Thus Midazolam-Propofol group was cost effective in induction of general anaesthesia, but we found Propofol-Propofol auto coinduction group showed stable hemodynamics than other groups. We also observed that after 10 minutes of intubation there was no difference between groups.

SUMMARY

This study was done as a randomised single blinded trial, conducted in 90 patients of aged 18 – 60 years of both sexes belonging to ASA1 & 2 undergoing elective surgery. In this study we compared the total dose requirements of Propofol and hemodynamic effects of Midazolam-Propofol coinduction with Propofol-Propofol auto coindution with control group. We randomly allotted patients in 3 groups of 30 each.

- Total dose of Propofol required for induction of anaesthesia was reduced in Propofol-Propofol group and Midazolam-Propofol group compared to control group. Maximum reduction of induction dose of Propofol was observed in Midazolam-Propofol group.
- Hemodynamic alterations seen after induction and after intubation was observed in all groups. Incidence of hypotension after induction was least in Propofol-Propofol group compared to control group. Intubation response was found to be least in Propofol-Propofol group compared to control group.

CONCLUSION

We hereby conclude that the usage of coinduction agents decreases the dose of induction agents with better hemodynamics.

- Propofol- Propofol coinduction results in better hemodynamics than Midazolam-Propofol coinduction.
- Midazolam-Propofol coinduction reduces Propofol requirement in induction of general anaesthesia than Propofol-Propofol coinduction and was found to be cost effective.

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. S.Jamuna
Postgraduate MD (Anaesthesiology),
Madras Medical College,
Chennai – 600 003.

Dear Dr. S.Jamuna,

The Institutional Ethics Committee has considered your request and approved your study titled **Prospective randomized study comparing induction dose requirements and hemodynamic alterations of propofol-propofol coinduction with midazolam-propofol coinduction in elective surgeries No.38082014.**

The following members of Ethics Committee were present in the meeting held on 05.08.2014 conducted at Madras Medical College, Chennai-3.

1. Dr.C.Rajendran, M.D.,	: Chairperson
2. Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.R.Nandhini, M.D., Inst.of Pharmacology, MMC	: Member
5. Dr.G.Muralidharan, Director Incharge, Inst.of Surgery	: Member
6. Prof.K.Ramadevi, Director i/c, Inst.of Biochemistry, MMC	: Member
7. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
8. Prof.Tito, M.D., Director i/c, Inst.of Internal Medicine, MMC	: Member
9. Thiru S.Rameshkumar, Administrative Officer	: Lay Person
10. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
11. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PATIENT CONSENT FORM

Study Title :

A Prospective, randomized control study comparing induction dose requirements and hemodynamic alterations of midazolam propofol coinduction with propofol propofol coinduction using priming principle, in patients undergoing elective surgeries.

Study Center : Institute of Anaesthesiology and Critical Care,
Rajiv Gandhi Govt. General Hospital,
Madras Medical College,
Chennai - 3.

Participant Name : Age: Sex: I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Signature / thumb impression of patient
Patient name:

Signature of the investigator:

Date:
Place:

INFORMATION TO PARTICIPANTS

Investigator **:** Dr.JAMUNA.S

Name of the Participant:

Title :

A Prospective, randomized control study comparing induction dose requirements and hemodynamic alterations in midazolam propofol coinduction with propofol propofol coinduction using priming principle, in patients undergoing elective surgeries.

You are invited to take part in this research study. We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria .We want to compare and study the induction dose requirements and hemodynamic alterations in midazolam propofol coinduction with propofol propofol coinduction

What is the Purpose of the Research:

For elective surgeries, premedication with either midazolam or propofol given, followed by propofol induction and intubation. This study is done to compare midazolam propofol coinduction with propofol propofol coinduction, in patients undergoing elective surgery with respect to

1. Induction dose requirements of propofol,
2. Hemodynamic alterations,

The Study Design:

All the patients in the study will be divided into three groups.

Group1- Pre medication with inj. glycopyrrolate, inj.fentanyl followed by propofol induction.

Group 2- Pre medication with inj. glycopyrrolate, inj. fentanyl, midazolam followed by propofol induction.

Group 3- Pre medication with inj.glycopyrrolate, inj.fentanyl, propofol followed by propofol induction.

Benefits

Premedication with midazolam /propofol

1. Reduces propofol induction dose requirements
2. Decreases the hemodynamic alterations
3. Reduces the side effects of propofol

Discomforts and risks

Hypotension, bradycardia may occur – emergency drugs are readily available

Apnoea can occur - patient manually ventilated

Allergic reactions may occur

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time :
Date :
Place :

Signature / Thumb Impression of Patient
Patient Name :

Signature of the Investigator : _____

Name of the Investigator : _____

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சியாளர் பெயர் : மருத்துவர். ஜமுனா.S.

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சி தலைப்பு

அறுவை சிகிச்சை முழுமயக்கம் தூண்டலுக்கு (Induction) அளிக்கப்படும் புரப்போஃபால் - புரப்போஃபால் மற்றும் மிடாசோலம் - புரப்போஃபால் மருந்துகளின் அளவு மற்றும் இரத்த ஓட்ட மாற்றங்களை ஒப்பிடுதல்

ஆராய்ச்சியின் நோக்கம்

இவ்வாராயச்சியில் அறுவை சிகிச்சைக்கு முழுமயக்கம் தூண்டலுக்கு அளிக்கப்படும் புரப்போஃபால் மற்றும் மிடாசோலம் மருந்துகளை செலுத்திய பின்னர் அறுவை சிகிச்சை செய்வதை கீழ்க்கண்ட கோணங்களில் ஒப்பிடப்படுகிறது.

1 புரப்போஃபால் தூண்டல் அளவு

2 இரத்த ஓட்ட மாற்றங்கள்

ஆய்வின் தன்மை

பங்கு பெறும் நோயாளிகள் மூன்று குழுக்களாகப் பிரிக்கப்படுவர்

குழு - 1 புரப்போஃபால் மூலமாக முழு மயக்கம் தூண்டப்படல்

குழு - 2 மிடாசோலம் செலுத்திய பின்பு புரப்போஃபால் மூலமாக முழுமயக்கம் தூண்டப்படல்

குழு - 3 புரப்போஃபால் செலுத்திய பின்பு புரப்போஃபால் மூலமாக முழுமயக்கம் தூண்டப்படல்

அறுவை சிகிச்சையின் போது இரத்த அழுத்தம், நாடித்துடிப்பின் மாற்றங்கள் கண்காணிக்கப்படும்.

நன்மைகள்

1. புரப்போஃபாலின் தூண்டல் அளவு குறைதல் மற்றும் அதனால் ஏற்படும் இரத்த அழுத்தம், நாடித்துடிப்பு மாற்றங்கள் சீராக இருக்கும்
2. உபாதைகள் குறைக்கப்படும்.
3.குறைந்த செலவு

ஏற்பாடும் உபாதைகள்

குறைந்த இரத்த அழுத்தம் குறைந்த நாடித்துடிப்பு ஏற்படலாம். அதற்கு மாற்று மருந்துகள் உடனடியாகக் கொடுக்கப்படும்

நீங்கள் இந்த ஆய்வில் பங்கு கொள்ள விருப்பமில்ஐ என்றால் எப்போதும் உபயோகப்படுத்தப்படும் முறையில் மருந்து கொடுக்கப்படும் உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

சாட்சியின் கையொப்பம்

பெயர்

பங்கு பெறுபவரின் கையொப்பம்
இடது கட்டைவிரல் ரேகை
பெயர்

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு

அறுவை சிகிச்சை முழுமயக்கம் தூண்டலுக்கு (Induction) அளிக்கப்படும் புரப்போஃபால் - புரப்போஃபால் மற்றும் மிடாசோலம் - புரப்போஃபால் மருந்துகளின் அளவு மற்றும் இரத்த ஓட்ட மாற்றங்களை ஒப்பிடுதல்

ஆராய்ச்சி நிலையம் : மயக்கவியல் துறை, சென்னை மருத்துவக் கல்லூரி, சென்னை-600 003

பங்கு பெறுபவரின் பெயர் :

பாலினம் :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன் எந்த காரணத்தினாலோ எந்த கட்டத்திலும எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்று அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். ☐

அறுவை சிகிச்சை முழுமயக்கம் தூண்டலுக்கு (Induction) அளிக்கப்படும் புரப்போஃபால் - புரப்போஃபால் அல்லது மிடாசோலம் - புரப்போஃபால் மருந்து கலவைகளை செலுத்தி முழுமயக்கம் கொடுக்கப்படும் என்பதை அறிந்து கொண்டேன். இதனால் உடலுக்கு எந்தவிதமான உபாதைகளும் இருக்காது என்பதையும் அறிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற முழு மனதுடன் சம்மதிக்கின்றேன்.

நேரம் :

நாள் :

இடம் :

கலந்து கொள்பவரின் கைரேகை / கையொப்பம்
பெயர்

ஆய்வாளரின் கையொப்பம் :

ஆய்வாளர் பெயர் :

PROFORMA

DATE :

NAME :

AGE : SEX :

DIAGNOSIS :

SURGICAL PROCEDURE DONE :

WT : CVS : RS : CNS :

ABDOMEN :

AIRWAY : MMS : IID TMD

DENTITION :

PRE OP ASSESSMENT :

HISTORY : Any Co-morbid illness

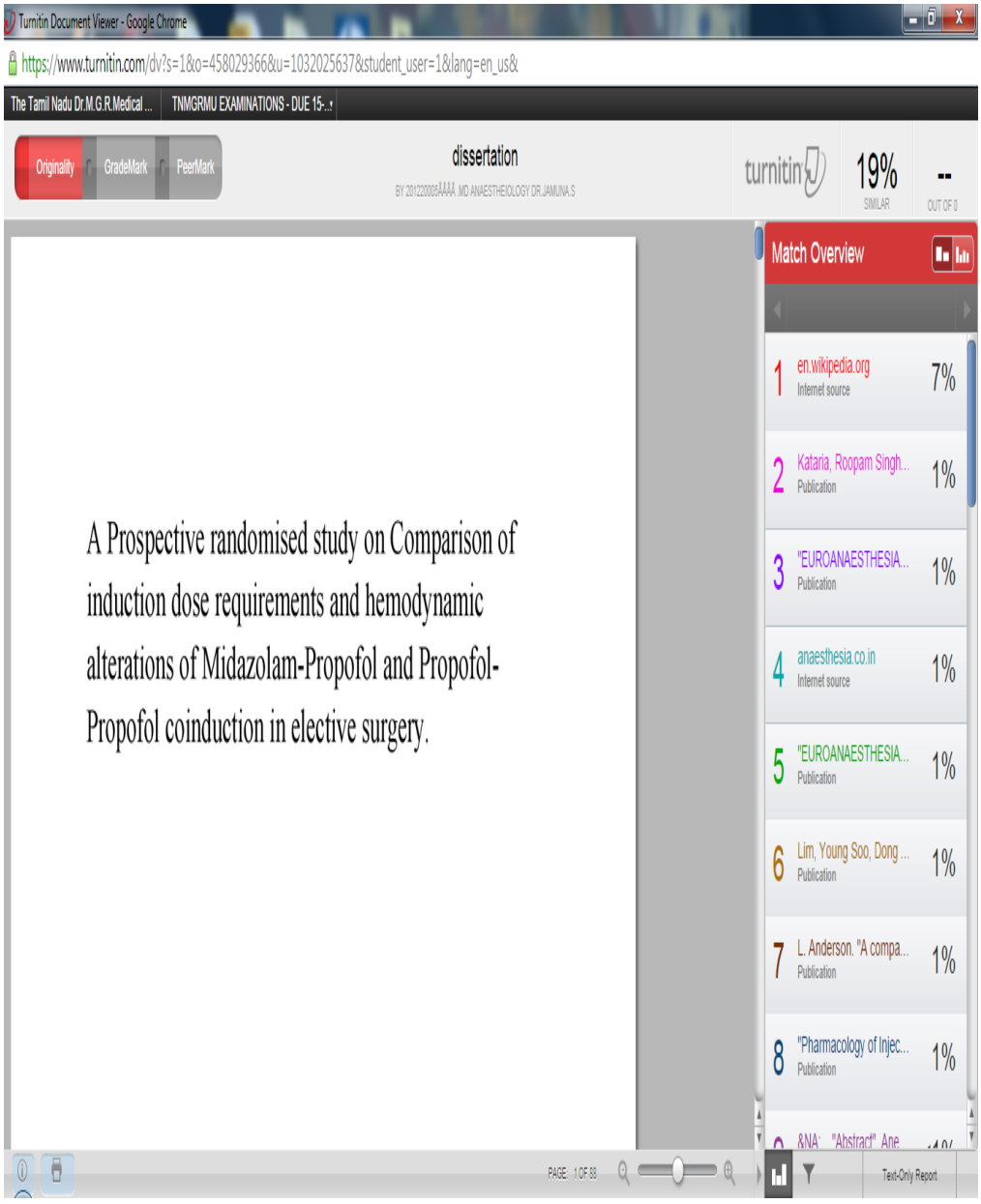
H/O Documented Difficult Airway

H/O previous surgeries

MEASURES OF STUDY OUTCOME :

	HR	SBP	DBP	MAP	SPO2
BASELINE					
BEFORE INDUCTION					
AFTER INDUCTION					
AFTER INTUBATION					
5 MINS AFTER INTUBATION					
10 MINS AFTER INTUBATION					

INDUCTION DOSE REQUIREMENTS OF THREE GROUPS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A Prospective randomised study on Comparison of induction dose requirements and hemodynamic alterations of Midazolam-Propofol and Propofol-Propofol combination in elective surgery.

MASTER CHART

SL.NO.	NAME	AGE	SEX	WEIGHT	PROCEDURE	ASA	GROUP	HR BASELINE	HR AFTER PREMEDICATION	HR AFTER INDUCTION	HR AFTER INTUBATION	HR AFTER 5 MINS	10 MINS	SBP BASELINE	SBP AFTER PREMEDICATION	SBP AFTER INDUCTION	SBP AFTER INTUBATION	SBP 5 MINS	SBP 10 MINS	DBP BASELINE	DBP AFTER PREMEDICATION	DBP AFTER INDUCTION	DBP AFTER INTUBATION	DBP 5 MINS	DBP 10 MINS	MAP BASELINE	MAP AFTER PREMEDICATION	MAP AFTER INDUCTION	MAP AFTER INTUBATION	MAP 5 MINS	MAP 10 MINS	SPO2	TOTAL DOSE OF PROPOFOL
	GROUP 1																															99	
1	BHAGYALAKSHMI	35	F	60	RIGHT PAROTIDECTOMY	2	1	74	70	62	90	90	78	110	108	90	130	130	124	74	72	58	90	92	90	86	84	68.66666667	103.3333333	104.6666667	101.3333333	99	120
2	MENAKA	55	F	54	LAP APPENDICECTOMY	2	1	88	84	74	110	88	80	120	122	100	120	110	110	80	84	64	92	95	90	93.33333333	96.66666667	76	101.3333333	100	96.66666667	99	100
3	SAVITHRI	60	F	50	COLOSTOMY	2	1	84	80	68	88	94	80	110	114	88	114	108	110	80	74	50	80	88	84	90	87.33333333	62.66666667	91.33333333	94.66666667	92.66666667	99	90
4	BALU	49	M	64	PARTIAL GASTRECTOMY	1	1	77	74	80	98	98	84	124	122	102	120	110	114	80	78	60	88	78	74	94.66666667	92.66666667	74	98.66666667	88.66666667	87.33333333	99	110
5	ANITHA	45	F	50	LAP CHOLECYSTECTOMY	1	1	98	94	82	110	92	88	130	128	114	130	120	110	90	88	64	90	94	90	103.3333333	101.3333333	80.66666667	103.3333333	102.6666667	96.66666667	99	100
6	RANI	60	F	50	LAP HERNIA REPAIR	1	1	110	98	90	114	110	90	130	134	108	110	110	110	90	82	68	90	88	90	103.3333333	99.33333333	81.33333333	96.66666667	95.33333333	96.66666667	99	90
7	ESWARAN	50	M	60	DIAGNOSTIC LAP	2	1	94	92	78	98	100	90	120	124	108	135	130	128	88	84	68	100	94	90	98.66666667	97.33333333	81.33333333	111.6666667	106	102.6666667	99	110
8	KANIMOZHI	43	F	50	TOTAL THYROIDECTOMY	1	1	78	74	72	100	98	80	110	114	90	124	110	106	70	68	54	84	80	82	83.33333333	83.33333333	66	97.33333333	90	90	99	100
9	NATARAJ	45	F	64	PAROTIDECTOMY	1	1	68	70	68	88	84	74	106	104	88	110	102	108	70	74	46	74	70	74	82	84	60	86	80.66666667	85.33333333	99	100
10	VIGNESH	30	M	70	LAP HERNIA REPAIR	1	1	84	82	78	98	94	78	110	112	94	70	100	106	72	64	62	78	74	80	84.66666667	80	72.66666667	75.33333333	82.66666667	88.66666667	99	100
11	VINOTHRAJ	34	M	72	OPEN CHOLECYSTECTOMY	1	1	114	104	100	118	110	90	134	134	118	138	120	118	90	92	70	98	92	80	104.6666667	106	86	111.3333333	101.3333333	92.66666667	99	90
12	SAKTHIVEL	25	M	64	LAP APPENDICECTOMY	1	1	90	88	74	100	104	94	110	110	90	112	100	104	78	74	68	80	78	74	88.66666667	86	75.33333333	90.66666667	85.33333333	84	99	100
13	CHELLAPPAN	50	M	60	OPEN CHOLECYSTECTOMY	1	1	84	84	74	100	104	92	108	104	92	120	120	110	70	68	58	85	80	70	82.66666667	80	69.33333333	96.66666667	93.33333333	83.33333333	99	110
14	SHUHAR	36	M	64	LAP CHOLECYSTECTOMY	1	1	88	90	94	110	110	100	120	122	108	124	110	108	80	80	74	88	88	74	93.33333333	94	85.33333333	100	95.33333333	85.33333333	99	120
15	RAMALINGAM	35	M	54	PARTIAL GASTRECTOMY	1	1	94	92	88	98	100	106	113	118	108	124	110	112	70	74	68	78	74	8080	84.33333333	88.66666667	81.33333333	93.33333333	86	5424	99	100
16	YESODHA	49	F	50	LEFT PAROTIDECTOMY	1	1	72	74	68	84	84	80	124	120	106	124	114	120	80	84	70	88	84	68	94.66666667	96	82	100	94	85.33333333	99	100
17	VANAJA	30	F	50	LAP APPENDICECTOMY	1	1	112	110	105	118	106	100	130	132	118	124	114	124	90	84	75	82	80	72	103.3333333	100	89.33333333	96	91.33333333	89.33333333	99	90
18	MOHANRAJ	60	M	60	SUBTOTAL GASTRCTOMY	2	1	100	98	88	98	94	92	128	124	108	130	124	122	90	88	80	90	88	74	102.6666667	100	89.33333333	103.3333333	100	90	99	110
19	DEVAN	25	M	70	LAP APPENDICECTOMY	1	1	80	78	70	78	80	78	104	105	88	110	108	104	70	70	58	88	84	78	81.33333333	81.66666667	68	95.33333333	92	86.66666667	99	110
20	SUJATHA	22	F	50	LAP APPENDICECTOMY	1	1	76	74	62	82	84	82	110	114	92	110	108	104	74	74	58	78	84	76	86	87.33333333	69.33333333	88.66666667	92	85.33333333	99	90
21	ARJUN	33	M	60	LAP VARICOCELE	1	1	98	94	90	118	110	106	128	124	108	130	124	128	88	84	68	90	92	74	101.3333333	97.33333333	81.33333333	103.3333333	102.6666667	92	99	100
22	KALYAN	28	M	60	LAP HERNIA REPAIR	1	1	92	88	82	98	98	90	130	132	120	140	130	130	90	90	80	94	90	80	103.3333333	104	93.33333333	109.3333333	103.3333333	96.66666667	99	90
23	ANJALI	24	F	50	B/L FIBROADENOMA EXCISION	1	1	80	84	78	94	92	90	110	114	98	128	130	128	88	80	58	90	88	94	95.33333333	91.33333333	71.33333333	102.6666667	102	105.3333333	99	80
24	MOHAN	32	M	54	LAP CHOLECYSTECTOMY	1	1	72	68	64	82	80	80	105	108	94	125	132	130	70	64	58	84	84	94	81.66666667	78.66666667	70	97.66666667	100	106	99	100
25	MARIYAMMAL	36	F	64	TOTAL THYROIDECTOMY	1	1	68	64	67	88	74	70	104	104	88	110	114	112	60	64	50	80	78	88	74.66666667	77.33333333	62.66666667	90	90	96	99	100
26	SANJIVASAN	33	M	70	LAP VARICOCELE	1	1	76	74	72	78	71	70	110	114	100	118	110	110	74	74	64	80	74	84	86	87.33333333	76	92.66666667	86	92.66666667	99	80
27	JAYA	35	F	50	TOTAL THYROIDECTOMY	1	1	110	112	98	115	98	90	134	134	106	120	106	100	88	84	78	88	78	82	103.3333333	100.6666667	87.33333333	98.66666667	87.33333333	88	99	100
28	SARASWATHI	24	F	60	LAP APPENDICECTOMY	1	1	92	92	90	114	100	94	120	124	108	128	110	108	88	84	70	88	84	80	98.66666667	97.33333333	82.66666667	101.3333333	92.66666667	80.33333333	99	90
29	RANJITH	28	M	64	LAP APPENDICECTOMY	1	1	104	104	98	118	102	102	124	124	112	130	128	120	84	88	86	90	88	84	97.33333333	100	94.66666667	103.3333333	101.3333333	92.66666667	99	100
30	SELVAM	44	M	62	DIAGNOSTIC LAP	2	1	78	74	68	88	78	74	110	110	100	120	108	100	70	70	58	84	78	74	83.33333333	83.33333333	72	96	88	82.66666667	99	110

SL.NO.	NAME	AGE	SEX	WEIGHT	PROCEDURE	ASA	GROUP	HR BASELINE	HR AFTER PREMEDICATION	HR AFTER INDUCTION	HR AFTER INTUBATION	HR AFTER 5 MINS	10 MINS	SBP BASELINE	SBP AFTER PREMEDICATION	SBP AFTER INDUCTION	SBP AFTER INTUBATION	SBP 5 MINS	SBP 10 MINS	DBP BASELINE	DBP AFTER PREMEDICATION	DBP AFTER INDUCTION	DBP AFTER INTUBATION	DBP 5 MINS	DBP 10 MINS	MAP BASELINE	MAP AFTER PREMEDICATION	MAP AFTER INDUCTION	MAP AFTER INTUBATION	MAP 5 MINS	MAP 10 MINS	SPO2	TOTAL DOSE OF PROPOFOL
	GROUP 2																																
1	VENKATESAN	55	M	70	LEFT COLOSTOMY	1	2	84	80	92	108	90	92	110	102	94	128	120	124	64	60	54	80	81	78	79.33333333	74	67.33333333	96	94	93.33333333	99	40
2	DHANASEKAR	25	M	50	LAP CHOLECYSTECTOMY	1	2	74	68	88	100	84	82	113	100	97	123	114	106	65	53	62	84	82	78	81	68.66666667	73.66666667	97	92.66666667	87.33333333	99	40
3	NALINI	26	F	65	LAP CHOLECYSTECTOMY	1	2	78	84	92	104	90	88	118	110	110	120	110	114	78	74	70	80	78	74	91.33333333	86	83.33333333	93.33333333	88.66666667	87.33333333	99	60
4	JAYA	60	F	50	TOTAL THYROIDECTOMY	2	2	122	118	99	105	94	86	155	147	142	144	120	126	82	75	65	80	74	74	106.3333333	99	90.66666667	101.3333333	92.66666667	91.33333333	99	30
5	AMARAVATHY	60	F	80	TOTAL THYROIDECTOMY	2	2	92	88	90	114	94	90	131	110	110	130	128	122	85	70	72	80	82	80	100.3333333	83.33333333	84.66666667	96.66666667	97.33333333	94	99	30
6	PRASANNAKUMAR	32	M	80	LAP HERNIORRAPHY	1	2	79	75	74	82	78	74	135	110	110	130	128	120	88	78	60	84	84	80	103.6666667	88.66666667	76.66666667	99.33333333	98.66666667	93.33333333	99	40
7	SUREKA	20	F	50	LAP APPENDICECTOMY	1	2	114	97	96	116	94	91	119	112	110	123	114	108	81	71	70	84	80	74	93.66666667	84.66666667	83.33333333	97	91.33333333	85.33333333	99	30
8	MALLISHWARI	50	F	56	LAPCHOLECYSTECTOMY	1	2	108	90	90	92	90	90	130	118	112	140	132	110	88	82	64	90	90	88	102	94	80	106.6666667	97.33333333	95.33333333	99	30
9	SELVAM	11	M	55	LAP APPENDICECTOMY	1	2	105	98	94	110	94	96	128	118	114	132	124	120	84	86	88	95	94	90	98.66666667	96.66666667	96.66666667	107.3333333	104	100	99	50
10	VISHWAMMAL	45	F	70	SIMPLE MASTECTOMY	2	2	84	83	80	105	94	94	123	117	98	113	108	110	84	78	57	74	78	74	97	91	70.66666667	87	88	86	99	40
11	PAVITHRADEVI	34	F	55	HEMITHYROIDECTOMY	1	2	90	74	80	90	88	84	110	113	95	98	97	100	77	73	59	78	84	84	88	86.33333333	71	84.66666667	88.33333333	89.33333333	99	40
12	KARTHI	22	M	50	LAP APPENDICECTOMY	1	2	82	80	80	90	78	74	131	126	128	140	145	130	85	75	80	88	90	84	100.3333333	92	96	105.3333333	108.3333333	99.33333333	99	50
13	DHARMALINGAM	57	M	50	LAP INGUINALHERNIA	2	2	77	74	74	88	74	70	124	118	114	128	124	126	84	72	74	88	92	78	97.33333333	87.33333333	87.33333333	101.3333333	106	94	99	40
14	KANCHANA	56	F	64	TOTAL THYROIDECTOMY	1	2	88	80	74	84	82	82	124	104	102	118	108	104	80	78	74	84	82	76	94.66666667	86.66666667	83.33333333	95.33333333	90.66666667	85.33333333	99	30
15	CHITRA	32	F	60	BILATERAL FIBROADENOMA	1	2	84	74	68	80	74	72	108	100	94	120	124	110	78	74	64	80	84	74	88	82.66666667	74	93.33333333	97.33333333	86	99	30
16	ELUMALAI	46	M	64	LAP HERNIORRAPHY	2	2	94	82	78	88	80	78	125	118	114	130	132	124	84	74	64	90	90	81	97.66666667	88.66666667	80.66666667	102.3333333	104	95.33333333	99	50
17	SUBRAMANI	60	M	60	LAP CHOLECYSTECTOMY	1	2	78	74	72	88	84	84	124	118	114	136	125	120	78	74	70	88	94	80	93.33333333	88.66666667	84.66666667	104	104.3333333	93.33333333	99	40
18	SURESH	24	M	68	LAP APPENDICECTOMY	1	2	110	100	94	120	110	108	124	120	104	138	112	120	88	74	60	84	88	64	100	89.33333333	74.66666667	102	96	82.66666667	99	50
19	SUJATHA	35	F	70	LAP INCISIONAL HERNIA REPAIR	1	2	104	88	84	97	94	92	130	110	104	120	102	104	88	72	64	90	82	70	102	84.66666667	77.33333333	100	88.66666667	81.33333333	99	30
20	RAJI	42	F	74	LAP INCISIONAL HERNIA REPAIR	1	2	88	84	74	98	84	80	110	108	100	125	108	110	68	64	58	84	84	78	82	78.66666667	72	97.66666667	92	88.66666667	99	50
21	MUNIAMMAL	34	F	64	TOTAL THYROIDECTOMY	1	2	74	72	64	88	78	74	104	100	95	112	110	114	74	62	58	84	84	74	84	74.66666667	70.33333333	93.33333333	92.66666667	87.33333333	99	40
22	RASI	50	F	58	TOTAL THYROIDECTOMY	1	2	108	98	88	102	100	100	124	110	104	130	120	124	74	68	68	84	86	78	90.66666667	82	80	99.33333333	97.33333333	93.33333333	99	50
23	TAMILSELVAN	34	M	62	SUBTOTAL GASTRECTOMY	1	2	90	80	68	110	98	92	110	108	100	128	110	110	74	72	68	84	90	80	86	84	78.66666667	98.66666667	96.66666667	98	99	30
24	KALI	33	M	70	LAP VARICOELE	1	2	98	88	84	94	98	92	124	120	108	132	126	120	80	82	74	90	88	80	94.66666667	94.66666667	85.33333333	104	100.6666667	93.33333333	99	40
25	KANIYAPPAN	45	M	65	OPEN CHOLECYSTECTOMY	1	2	78	74	68	88	84	78	110	104	104	124	114	116	78	74	70	88	84	86	88.66666667	84	81.33333333	100	94	96	99	60
26	MURUGESAN	64	M	70	LAP HERNIA REPAIR	1	2	90	84	82	94	90	88	112	106	102	128	112	110	74	76	64	84	76	74	86.66666667	86	76.66666667	98.66666667	88	86	99	40
27	DAISHAYINI	58	F	50	TOTAL THYROIDECTOMY	2	2	84	78	70	92	94	98	128	124	110	138	130	126	84	82	78	94	74	70	98.66666667	96	88.66666667	108.6666667	92.66666667	88.66666667	99	50
28	STALIN	60	M	50	COLOSTOMY	2	2	110	88	84	98	100	104	132	120	110	138	134	120	90	80	74	90	74	72	104	93.33333333	86	106	94	88	99	40
29	NISHA	32	F	60	LAP APPENDICECTOMY	1	2	74	68	64	80	88	84	110	101	94	128	110	106	78	74	68	82	70	68	88.66666667	83	76.66666667	97.33333333	93.33333333	80.66666667	99	30
30	RAMU	40	M	60	LAP CHOLECYSTECTOMY	1	2	80	74	68	88	84	76	106	100	94	114	105	100	68	64	54	86	68	64	80.66666667	76	67.33333333	95.33333333	80.33333333	76	99	30

SL.NO.	NAME	AGE	SEX	WEIGHT	PROCEDURE	ASA	GROUP	HR BASELINE	HR AFTER PREMEDICATION	HR AFTER INDUCTION	HR AFTER INTUBATION	HR AFTER 5 MINS	10 MINS	SBP BASELINE	SBP AFTER PREMEDICATION	SBP AFTER INDUCTION	SBP AFTER INTUBATION	SBP 5 MINS	SBP 10 MINS	DBP BASELINE	DBP AFTER PREMEDICATION	DBP AFTER INDUCTION	DBP AFTER INTUBATION	DBP 5 MINS	DBP 10 MINS	MAP BASELINE	MAP AFTER PREMEDICATION	MAP AFTER INDUCTION	MAP AFTER INTUBATION	MAP 5 MINS	MAP 10 MINS	SPO2	TOTAL DOSE OF PROPOFOL
	GROUP 3																													0		99	
1	JOHN	52	M	60	LAP APPENDICECTOMY	1	3	64	64	72	68	64	68	124	110	109	126	124	110	82	65	64	78	74	78	96	80	79	94	90.66666667	93.33333333	99	60
2	LATHA	30	F	65	TOTAL THYROIDECTOMY	1	3	82	74	67	84	84	80	140	120	120	130	130	120	82	68	57	84	78	80	101.3333333	85.33333333	78	99.33333333	95.33333333	96.66666667	99	70
3	NEELAVATHY	32	F	67	LAP INCISIONAL HERNIA REPAIR	2	3	78	72	64	68	74	72	124	117	107	122	120	124	86	67	64	84	80	87	98.66666667	83.66666667	78.33333333	96.66666667	93.33333333	98	99	80
4	BEGLIRAJ	58	M	70	LAP HERNIORAPPHY	1	3	88	84	82	80	78	76	134	130	124	114	110	111	84	84	82	84	80	80	100.6666667	99.33333333	96	94	90	90	99	70
5	SATHISH	21	M	55	LAP HERNIA REPAIR90	1	3	90	78	74	87	84	82	132	125	119	123	120	120	80	78	74	80	74	78	97.33333333	93.66666667	89	94.33333333	89.33333333	92	99	80
6	CHANDRASEKAR	48	M	70	LAP HERNIA REPAIR	1	3	72	69	58	63	64	68	121	101	98	91	90	100	81	66	65	64	64	70	94.33333333	77.66666667	76	73	72.66666667	76.66666667	99	100
7	SARAVANAN	41	M	70	LAP APPENDICECTOMY	1	3	88	84	86	86	84	76	100	98	92	94	90	98	72	74	64	64	64	70	81.33333333	82	73.33333333	74	72.66666667	76.66666667	99	50
8	PANNERSELVAM	35	M	70	LAP APPENDICECTOMY	1	3	74	72	80	84	80	78	125	112	110	130	120	112	82	67	74	88	78	88	96.33333333	82	86	102	92	98.66666667	99	80
9	PARVATHY	67	F	60	OPEN CHOLECYSTECTOMY	2	3	108	97	100	107	106	106	140	133	124	128	110	108	90	88	84	90	84	98	106.6666667	103	97.33333333	102.6666667	92.66666667	102	99	80
10	RANI	35	F	50	R HEMITHYROIDECTOMY	1	3	107	82	84	90	90	88	121	112	110	110	104	102	77	61	63	78	80	88	91.66666667	78	78.66666667	92	88	93.33333333	99	80
11	URAMMA	60	F	50	OPEN CHOLECYSTECTOMY	2	3	107	105	84	90	88	84	132	124	119	132	106	100	75	74	60	68	70	70	94	94	79.66666667	86	82	82	99	60
12	SUSEELA	50	F	65	LAP CHOLECYSTECTOMY	1	3	76	68	64	74	72	70	134	117	107	121	108	100	84	74	68	74	78	74	100.6666667	88.33333333	81	89.66666667	88	85.33333333	99	40
13	LOGAVEERAN	20	M	50	LAP APPENDICECTOMY	1	3	108	112	84	90	90	84	124	114	94	88	80	94	84	68	74	72	70	74	97.33333333	83.33333333	80.66666667	77.33333333	73.33333333	76	99	70
14	SUREKA	24	F	40	LAP APPENDICECTOMY	1	3	114	97	96	110	108	100	119	122	110	124	106	100	81	74	70	84	80	80	93.66666667	86.66666667	83.33333333	97.33333333	88.66666667	88.66666667	99	60
15	MAHENDRABABU	31	M	65	LAP VARICOCELE	1	3	66	64	62	64	68	67	121	112	108	118	102	98	78	68	74	80	84	78	92.33333333	82.66666667	85.33333333	92.66666667	90	86	99	70
16	DIANA	20	F	50	LAPAPPENDICECTOMY	1	3	93	87	88	94	90	87	109	109	98	102	94	100	74	64	58	64	70	68	85.66666667	79	71.33333333	76.66666667	78	76.66666667	99	50
17	JAYALAKSHMI	48	F	74	R MASTECTOMY	1	3	90	98	94	100	100	90	122	120	118	114	106	108	74	78	70	78	78	74	90	92	86	90	87.33333333	84.66666667	99	70
18	KARPAGAVALLI	38	F	50	LAP CHOLECYSTECTOMY	1	3	108	98	94	98	100	94	124	120	112	120	108	110	78	74	62	78	80	78	93.33333333	89.33333333	78.66666667	92	89.33333333	88	99	60
19	JAYA	55	F	70	R SUBMANDIBULAR EXCISION	1	3	112	96	94	105	102	94	139	108	100	134	120	120	90	62	70	88	82	80	106.3333333	77.33333333	80	103.3333333	94.66666667	93.33333333	99	80
20	BALAMURUGAN	27	M	60	OPEN CHOLECYSTECTOMY	1	3	94	92	85	104	100	98	134	121	111	135	130	128	74	78	70	78	80	78	94	92.33333333	83.66666667	97	90.66666667	95.33333333	99	60
21	PONNAMMAL	65	F	55	LAP CHOLECYSTECTOMY	2	3	120	108	98	105	100	94	130	104	124	128	134	130	90	80	75	80	80	80	103.3333333	88	91.33333333	96	98	98	99	80
22	RATHI	24	F	54	LAP APPENDICECTOMY	1	3	110	100	94	114	104	100	124	110	104	112	120	120	84	67	76	84	78	78	97.33333333	94.66666667	85.33333333	93.33333333	92	92	99	80
23	VARADHAN	50	M	72	TOTAL THYROIDECTOMY	1	3	84	74	82	88	90	94	120	107	112	120	110	111	80	74	76	80	74	76	93.33333333	85	88	93.33333333	86	87.33333333	99	70
24	BALASUNDARAM	54	M	60	TOTAL THYROIDECTOMY	2	3	74	70	74	78	88	84	120	118	110	128	120	122	80	74	70	80	74	70	93.33333333	88.66666667	83.33333333	96	89.33333333	86.66666667	99	70
25	JANAKI	45	F	60	LAP CHOLECYSTECTOMY	1	3	88	80	74	78	74	79	112	110	106	118	110	110	70	74	60	78	72	70	84	86	75.33333333	91.33333333	84.66666667	83.33333333	99	80
26	LAKSHMI	26	F	70	LAP APPENDICECTOMY	1	3	92	84	74	80	78	74	118	114	104	118	106	104	78	70	64	82	70	70	91.33333333	84.66666667	77.33333333	94	82	82	99	70
27	BALAJI	34	M	54	LAP HERNIA REPAIR	2	3	110	108	104	110	108	104	130	124	118	124	118	120	84	882	68	80	74	72	99.33333333	629.3333333	84.66666667	94.66666667	88.66666667	87.33333333	99	80
28	KAMARAJ	50	M	60	RIGHT PAROTIDECTOMY	1	3	78	70	74	76	78	74	110	104	94	98	98	94	80	84	74	70	78	74	90	90.66666667	80.66666667	79.33333333	84.66666667	82	99	60
29	SELVA	65	M	70	LAP HERNIA REPAIR	1	3	68	64	68	78	74	70	104	100	92	114	108	100	68	64	54	74	72	70	80	76	66.66666667	87.33333333	83.33333333	82.66666667	99	50
30	ARUMUGAM	22	M	50	LAP APPENDICECTOMY	1	3	80	74	74	78	74	72	124	110	110	114	110	106	74	78	64	82	78	74	90.66666667	92	79.33333333	92.66666667	88.66666667	86	99	60